Total testosterone level may have no influence on the occurrence and severity of erectile dysfunction in males aged between 30 and 60 years living with type 2 diabetes

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Background: Erectile dysfunction is the most common sexual disorder in type 2 diabetes. Its pathogenesis may involve various disturbances including endothelial dysfunction and dysautonomia. The involvement of a low testosterone level is still debated. The aim of this study was to evaluate the contribution of total testosterone during erectile dysfunction in patients living with type 2 diabetes.

Method: A cross-sectional study was conducted in a population of male with type 2 diabetes, aged 30–60 years, and enrolled at the National Obesity Centre of the Yaoundé Central Hospital. Non-diabetic conditions that could affect testosterone level were excluded. Erectile dysfunction was assessed using the IIEF-5 questionnaire. Total testosterone was measured by ELISA. The relationship between erectile dysfunction and total testosterone has been explored through correlation using Pearson’s coefficient. The significance threshold was set at 0.05.

Results: A total of 83 participants were included, with an average age of 47.9 ± 7.8 years. The median duration of diabetes was 24 (5; 72) months. The frequency of ED was 65.1%, severe for 50% of cases and significantly associated with the duration of diabetes (OR = 7.5 [2.4; 22.8]). The mean testosterone level was 14.3 ± 5.1 nmol/l. A low level of testosterone was found in 8.4% (7/83) of participants, and sedentary lifestyle was significantly associated with low testosterone level (OR = 4.1 [1; 15.4]). There was no difference between the mean total testosterone level of patients with ED (14.1 ± 4.7 nmol/l) and those without (14.3 ± 5.9 nmol/l) (p = 0.8). No association was found between total testosterone level and IIEF-5 score (r = −0.05; p = 0.5).

Conclusion: Erectile dysfunction occurs in two out of three people living with type 2 diabetes and is severe for half of the cases. Total testosterone level does not seem to have an influence on the onset or severity of ED in male under 60 years with type 2 diabetes, but it is associated with a sedentary lifestyle.

Keywords: erectile dysfunction, total testosterone level, type 2 diabetes

Background

Erectile dysfunction (ED) is defined as the permanent and recurrent inability to achieve and maintain an erection sufficient for satisfactory sexual intercourse. 1 It is a widespread condition worldwide and its prevalence varies from one population to another. In the United States, the Massachusetts Male Aging Study (MMAS) found a 52% prevalence of ED in men aged 40–70 years. 2 It is an under-diagnosed condition because, as it is still considered a ‘taboo’ subject, patients tend not to bring it up spontaneously in front of their doctor. 3 Diao et al. in Senegal and Oyelade et al. in Nigeria have reported community prevalences of 26% and 58.9% respectively. 4,5 An essential aspect of the condition is that it alters the quality of life of men who suffer from it, leading to often invisible psychological distress in the form of marital conflict, low self-esteem and a sense of failure as a man. 6 The mechanisms contributing to ED in diabetes are multiple, including autonomic neuropathy, endothelial dysfunction and sometime iatrogenic causation by multiple medications and psychological disorders such as mental depression, which is not rare in type 2 diabetes (T2DM) patients. 7

In fact, ED affects one in two patients with diabetes, which is four times higher than that of the general population. 8 Most recent studies in Africa show prevalence rates of 50%. 9,10 The number of people living with T2DM and diagnosed with ED increases significantly with duration of T2DM, age, poor glycaemic control, and is correlated with the occurrence of chronic complications of T2DM, particularly cardiovascular, renal and neurological complications. 11 A low testosterone level is classically recognised as a physiological mechanism of ED occurring with age in patients without diabetes. It was found in 20% of T2DM patients below the age of 60 by Kapoor et al., highlighting its possible contribution to the pathogenesis of ED. 12 However, its involvement is still debated and subject to controversy. The aim of this study was to evaluate the contribution of testosterone level in a population of Cameroonian patients living with T2DM and ED.
Methods

Study design and setting
We carried out a cross-sectional study at the National Obesity Center of the Yaoundé Central Hospital (HCV). This is a tertiary and referral hospital in the urban city of Yaoundé. There are several specialised services, including the Endocrinology Department and the National Obesity Centre, from which we recruited participants. Our study ran from November 2019 to June 2020.

Participants
We included adult males aged between 30 and 60 years, living with type 2 diabetes on an outpatient basis. We excluded from the study participants with known abnormalities in sexual differentiation; with a known history of a condition that may cause erectile dysfunction such as chronic kidney disease, dysthyroidism, chronic liver disease; or who had undergone genitourinary tract surgery, or follow-up for prostate pathology.

We also excluded participants who were taking a drug that may promote erectile dysfunction such as beta-blockers, spironolactone and psychotropic drugs at the time of the study, and those already receiving treatment for a previous diagnosis of erectile dysfunction. We also excluded participants with a glomerular filtration rate of less than 30 ml/minute, and/or an alanine amino transferase value greater than three times normal.

Sample size estimation
We used the sample size formula for a difference in mean between groups, described in the Witheley and Ball manual.13 Our hypothesis was a 20% difference in total testosterone between patients with T2D and ED and those without. Given the mean total testosterone level of patient with T2D without erectile dysfunction incoming from Mushtaq et al. of 21.6 ± 3.9 nmol/l14 and an estimated 20% difference in total testosterone, an estimated sample size of 22 participants for each group (with and without ED) was calculated using Whitley and Ball (2002).13 We proceeded by a consecutive sampling.

Data assessment
We used a data collection form to collect data on age, professional and marital status, history of diabetes (month and year of diagnosis, regularity of consultations, chronic complications of diabetes, current treatment, and glycated haemoglobin less than six months old); relevant history (hypertension, hyperthyroidism, chronic at-risk consumption of tobacco and/or alcohol, HIV infection, chronic viral hepatitis).

We evaluated erectile dysfunction using the IIEF-5 questionnaire (five-item version of the International Index of Erectile Function). This is a five-item self-administered questionnaire with answers rated from zero to five. It evaluates sexual function over a period of at least six months and takes into account sexual desire (question 1), erection (questions 2, 3 and 4) and sexual satisfaction (question 5). It is rated from 1 to 25; the participant had erectile dysfunction if the score varied between 5 and 20. In general we considered the scores to show severe erectile dysfunction (5–10); moderate (11–15); mild (16–20); normal result (21–25); non-interpretable result (1–4). Participants with uninterpretable results were excluded. The questionnaire was self-administered by each participant. Blood pressure, abdominal circumference and determined body mass index using weight and height were measured.

All blood samples were collected in the morning between 8 and 10 am respecting the circadian rhythm of testosterone secretion and after a fasting period of at least 6 hours. The last meal was ingested at 8 pm the day prior to blood sample collection. Then, we determined the testosterone level in the blood samples using the competitive enzyme-linked immunoabsorbent assay.

Serum creatinine was determined and estimated glomerular filtration rate was calculated using the MDRD formula.

Operational terms
A low testosterone level was defined according to the Endocrine Society of Clinical Practice Guideline criteria, by a serum total testosterone (TT) value less than or equal to 8 nmol/l. Values above 12 nmol/l are considered normal; those between 8 and 12 nmol/l are considered borderline testosterone levels.12 Male hypogonadism was defined as the presence in men of symptoms/signs of androgen deficiency such as ED, combined with biochemical evidence of this deficiency. It is said to be straightforward for a testosterone level ≤ 8 nmol/l with or without ED, and borderline for a testosterone between 8 and 12 nmol/l with ED.

Statistical analysis
All the data collected were analysed using the software SPSS (Statistical Package for Social Sciences) version 23.0 (IBM Corp, Armonk, NY, USA). Quantitative variables were expressed in terms of mean and standard deviation (SD) or median with the interquartile range (Q25; Q75), while qualitative variables were expressed as counts and proportions. The comparison of the means of the quantitative variables between two groups was done using Student’s t-test. Factors associated with ED and testosterone level were determined using Fisher’s exact test. The odds ratio (OR) and its 95% confidence interval were used to quantify the degree of association. The relationship between ED (evaluated by the IIEF-5 score) and total testosterone level has been tested through correlation and presented with the Pearson correlation coefficient. The significance threshold was set at 0.05.

Ethical approval
We obtained authorisation from Yaoundé Central Hospital and ethical approval from the Institutional Ethical Review Board of the Faculty of Medicine of Biomedical Sciences of the University of Yaoundé 1 (No. 343/UY1/FMSB/VDR/DAASR/CSD).

Results

Characteristics of the sample
Overall, 83 participants were recruited. The average age of participants was 47.9 ± 7.8 years, with extremes of 31 and 60 years. Some 73.5% of participants had a sedentary lifestyle and 71.1% regularly drank alcohol. Sixteen participants (19.3%) had hypertension. The median of the duration of diabetes since diagnosis was 24 (5; 72) months. Most participants (77.1%) kept their follow-up appointments regularly. Pharmacological treatments for diabetes included oral antidiabetic drugs in 72.3% of cases, and/or insulin in 37.3% of cases. The mean HbA1c of participants was 7.9 ± 2.1%. Thirty-five participants (42.2%) had strict control (HbA1c < 7%). Chronic complications were found in 17 (20.5%) participants. These were mainly diabetic foot (11 participants). The mean BMI was 26.4 ± 4.1 kg/m². In total, 38 patients were overweight (45.8%). The characteristics of the sample are presented in Table 1.
Our results show that ED was present in 54/83 participants (65.1%). Nisahan et al. and Cho et al. had a prevalence of 62.9% and 65.5%, meaning that ED in T2DM is encountered in one patient in two, arising as a frequent complication in males with T2DM and representing an important issue to be assessed. Factors associated with ED in the sample included: age above 48 years (OR = 2.7 [1.08; 7]), duration of diabetes of at least 24 months (OR = 7.5 [2.4; 22.8]) and the presence of chronic complications of T2DM (OR = 11.7 [1.4; 94]) (Table 2).

### Frequency of low testosterone level and its contribution to erectile dysfunction

The mean testosterone level in the sample was 14.3 ± 5.1 nmol/l. Low testosterone level was found in 21 (25.3%) participants. Sedentary lifestyle was the only factor associated with low testosterone level (OR = 4.1 [1; 15.4], p = 0.03) (Table 3). There was no significant difference between the mean total testosterone levels of patients with ED (14.1 ± 4.7 nmol/l) and those without (14.3 ± 5.9 nmol/l) (Figure 1).

## Discussion

The present study assessed the contribution of testosterone in erectile dysfunction in patients living with T2DM. Testosterone is the main androgen in male responsible for sex differentiation of external genitals. It is also useful in the triggering and maintenance of erectile function. ED in T2DM is generally a consequence of the low level of NO resulting in an endothelial dysfunction in the intracavernous tissues. Efficient treatment of ED could improve patients’ quality of life. A low testosterone level could be apparent as a remediable cause of ED and for this reason it should be assessed. We measured total testosterone using the immuno-assay method. Although liquid chromatography coupled with mass spectrometry (LC-MS/MS) is the method recommended by the Endocrine Society for determination of androgens, it is more expensive and labour-intensive so that it cannot be easily applicable for cohort studies. Some authors recommend immunoassay in routine assessment of total testosterone. This method is equal and has a sensibility comparable to LC-MS/MS.

Our results show that ED was present in 54/83 participants (65.1%). Nisahan et al. and Cho et al. had a prevalence of 62.9% and 65.5%, meaning that ED in T2DM is encountered in one patient in two, arising as a frequent complication in males with T2DM and representing an important issue to be assessed. Factors associated with ED in the sample included: age above 48 years (OR = 2.7 [1.08; 7]), duration of diabetes of at least 24 months (OR = 7.5 [2.4; 22.8]) and the presence of chronic complications of T2DM (OR = 11.7 [1.4; 94]). All these factors are generally correlated to poor diabetes control.

There was no statistically significant difference between the mean total testosterone levels of patients with ED (14.1 ± 4.7 nmol/l) and those without ED (14.3 ± 5.9 nmol/l) (p = 0.3). This suggests that serum total testosterone levels do not

### Table 1: Baseline characteristics of the sample

| Variables                    | Overall (n = 83) | Percentages |
|------------------------------|-----------------|-------------|
| n (%)                        | 83              | 100         |
| Mean age, year (SD)          | 47.9 (7.8)      |             |
| Age, min–max, year           | 31–60           |             |
| Comorbidities:               |                 |             |
| Physical inactivity          | 61              | 73.5        |
| Alcoholism                   | 59              | 71.1        |
| Active smoking               | 24              | 28.9        |
| High blood pressure          | 16              | 19.3        |
| HIV infection                | 2               | 2.4         |
| Body mass index:             |                 |             |
| Underweight                  | 2               | 2.4         |
| Normal                       | 33              | 39.8        |
| Overweight                   | 38              | 45.8        |
| Obesity                      | 10              | 12          |
| Abdominal obesity            | 9               | 10.8        |
| Diabetes control (HbA1c):    |                 |             |
| ≤ 7%                         | 35              | 42.2        |
| 7%–8.5%                      | 21              | 25.3        |
| > 8.5%                       | 27              | 32.5        |
| Vascular complications:      |                 |             |
| Stroke                       | 1               | 1.2         |
| Diabetic foot                | 11              | 13.3        |
| Diabetic retinopathy         | 7               | 8.4         |

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**Table 2: Factors associated with erectile dysfunction in the sample**

| Erectile dysfunction | Yes (n = 54) | No (n = 29) | OR [IC 95%]   | p-value | p-value | aOR [95% CI] |
|----------------------|-------------|-------------|---------------|---------|---------|--------------|
| Age ≥48 years        | 32 (76.2)   | 10 (23.8)   | 2.7 [1.08; 7] | 0.04    | 0.2     | 1.9 [0.6; 5.4] |
| HbA1c ≥ 8%           | 25 (67.6)   | 12 (32.4)   | 1.2 [0.4; 3]  | 0.8     | –       | –            |
| Duration of diabetes ≥24 months | 33 (86.8) | 5 (13.2) | 7.5 [2.4; 22.8] | < 0.001 | 0.005 | 5.2 [1.6; 16.5] |
| BMI ≥ 25 kg/m²       | 28 (58.3)   | 20 (41.7)   | 0.4 [0.1; 1.2] | 0.1     | –       | –            |
| Abdominal obesity    | 7 (77.8)    | 2 (22.2)    | 2.0 [0.3; 10.3] | 0.4     | –       | –            |
| High blood pressure  | 13 (81.3)   | 3 (18.8)    | 2.7 [0.7; 10.5] | 0.1     | –       | –            |
| Complications of diabetes | 16 (94.1) | 1 (5.9) | 11.7 [1.4; 94] | 0.004   | 0.1     | 5.8 [0.6; 51] |
| Physical inactivity  | 42 (68.9)   | 19 (31.1)   | 1.8 [0.6; 5]  | 0.2     | –       | –            |
| Alcohol consumption  | 39 (66.1)   | 20 (33.9)   | 1.1 [0.4; 3.1] | 0.8     | –       | –            |
| Tobacco consumption  | 19 (79.2)   | 5 (20.8)    | 2.6 [0.8; 7.9] | 0.1     | –       | –            |
| Insulin treatment    | 21 (67.7)   | 10 (32.3)   | 1.2 [0.4; 3]  | 0.8     | –       | –            |

*aOR: adjusted Odd Ratio; HbA1c: glycated hemoglobin; BMI: body mass index. Statistical significance: p < 0.05*
influence the occurrence of ED in T2DM. Kapoor et al. found similar results: there were no significant differences in total testosterone levels in men with and without ED (total testosterone $12.5 \pm 0.09$ versus $12.7 \pm 0.08$ nmol/l, $p = 0.1$). However, a study published in Egypt found that patients with ED had lower total testosterone than those without ED. To justify this disparity of results, the hypothesis put forward would be the concomitant drop in SHBG levels, frequently observed during diabetes, reducing serum transport and therefore testosterone bioavailability.

The physiological role of SHBG would be more complex than the simple transport of sex hormones, and would also intervene in the physiopathology of insulin resistance during T2DM. In relation to our results, a meta-analysis concluded that, in the majority of cases, ED in T2DM and its severity are due to neuropathy and vasculopathy and not due to hormonal problems, as confirmed by numerous published studies. Low testosterone level was found only in 8.4% (7/83) of the whole sample. Although testosterone does not influence the occurrence of erectile dysfunction in T2DM patients, sedentary lifestyle was a factor associated with low testosterone level in T2DM with ED (OR = 4.1 [1; 15.4], $p = 0.03$). In fact, there is a relation between BMI and testosterone level. Physical activity improves bioavailability of testosterone by dropping the level of SHBG.

Table 3: Factors associated with a decrease in total testosterone level

| Variables                        | Testosterone level | p-value | OR [95% CI] |
|----------------------------------|--------------------|---------|-------------|
|                                 | < 12 nmol/l | ≥ 12 nmol/l |         |             |
| Age ≥ 48 years                   | $n = 27$     | $n = 56$     | 0.6     | 1.3 [0.5; 3.3] |
| Duration diabetes > 24 months   | $n = 27$     | $n = 56$     | 0.3     | 0.5 [0.2; 1.5] |
| BMI ≥ 25kg/m²                    | $n = 27$     | $n = 56$     | 0.8     | 0.8 [0.3; 2.2] |
| Abdominal obesity                | $n = 27$     | $n = 56$     | 0.1     | 2.9 [0.7;12]  |
| High blood pressure              | $n = 27$     | $n = 56$     | 0.07    | 0.2 [0.05;1.1] |
| Chronic complications            | $n = 27$     | $n = 56$     | 0.7     | 1.1 [0.3; 3.5] |
| Sedentary lifestyle              | $n = 27$     | $n = 56$     | 0.03    | 4.1 [1; 15.4]  |
| Alcohol consumption              | $n = 27$     | $n = 56$     | 0.1     | 0.4 [0.1; 1.1] |
| Tobacco consumption              | $n = 27$     | $n = 56$     | 0.1     | 0.4 [0.1; 1.3] |
| Insulin treatment                | $n = 27$     | $n = 56$     | 1       | 0.9 [0.3; 2.5] |

BMI: body mass index. Statistical significance: $p < 0.05$
which are mainly psychological, neurological and vascular, in diabetic patients before going through testosterone dosage, especially when they practise in the context of low-resource settings, where this examination is expensive for patients who are already under the burden of chronic medication.

Conclusion
Erectile dysfunction is common in patients living with type 2 diabetes, especially as the duration of diabetes goes beyond 24 months. Although a low level of testosterone is rarely found in this population, this hormonal status is associated with a sedentary lifestyle. Total testosterone level did not influence the occurrence and severity of erectile dysfunction in our study.

Abbreviations
BMI (body mass index); ED (erectile dysfunction); T2DM (type 2 diabetes mellitus), IIEF-5 (International Index of Erectile Function 5 item version), ELISA (enzyme-linked immunosorbent assay), SHBG (sex hormone binding globulin).

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References
1. Brock G, Harper W. Erectile dysfunction. Can J Diabetes. 2013;37: S150–2.
2. Feldman HA, Goldstein I, Hatzichristou DG, et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts male aging study. J Urol. 1994;151(1):54–61.
3. Rakovac Tisdal A, King TFJ, Mahmood WAW, et al. Erectile dysfunction: they don’t talk, we don’t ask. Diabet Med. 2018;35(5):667–8.
4. Diao B, Ndoye AK, Fall PA, et al. La dysfonction érectile au Sénégal: Profil épidémiologique. Andrologie. 2007;17(3):223–9.
5. Oyelade BO, Jemilohun AC, Adenibigbe SA. Prevalence of erectile dysfunction and possible risk factors among men of South-Western Nigeria: a population based study. Pan Afr Med J [Internet]. 8 juin 2016 [cité 23 juin 2020];24. Disponible sur: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5012735/.
6. Camara A, Baldé NM, Enoru S, et al. Prevalence of anxiety and depression among diabetic African patients in Guinea: association with HbA1c levels. Diabetes Metab. 2015;41(1):62–68.
7. Morano S. Pathophysiology of diabetic sexual dysfunction. J Endocrinol Invest. 2003;26(3 Suppl):65–9.
8. Walle B, Lebeta KR, Fita YD, et al. Prevalence of erectile dysfunction and associated factors among diabetic men attending the diabetic clinic at Felege Hiwot Referral Hospital, Bahir Dar, North-West Ethiopia, 2016. BMC Res Notes. 2018;11(1):130.
9. Baldé NM, Diallo AB, Baldé MC, et al. Dysfonction érectile et diabète à Conakry (Guinée): fréquence et profil clinique à partir de 187 observations. Ann Endocrinol. 2006;67(4):338–42.
10. Zakhama W, Chaabouni A, Rzouga S, et al. Dysfonction érectile et diabète : fréquence et profil clinique à partir de 200 observations. Andrologie. 2012;22:96–101.
11. Furukawa S, Sakai T, Niya T, et al. Diabetic peripheral neuropathy and prevalence of erectile dysfunction in Japanese patients aged<65 years with type 2 diabetes mellitus: the Dogo study. Int J Impot Res. 2017;29(1):30–4.
12. Kapoor D, Aldred H, Clark S, et al. Clinical and biochemical assessment of hypogonadism in men with type 2 diabetes: correlations with bioavailable testosterone and visceral adiposity. Diabetes Care. 2007;30(4):911–7.
13. Whitley E, Ball J. Statistics review 4: sample size calculations. Crit Care. 2002;6:335.
14. Mushtaq S, Khan K, Abid S, et al. Frequency of hypogonadism and erectile dysfunction in type-II diabetic patients. Cureus [Internet]. [cité 5 nov 2019];10(5). Disponible sur: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6053255.
15. Czeloth K, Bobjør J, Bronton K, et al. Comparison of testosterone measurement by the new ‘gold standard’ method liquid chromatography tandem mass spectrometry versus the traditionally in clinical routine used immunoasays in the prediction of symptoms of male hypogonadism. Eur Urol Suppl. 2017;16(13):e3018.
16. Nisahan B, Kumanan T, Rajeshkannan N, et al. Erectile dysfunction and associated factors among men with diabetes mellitus from a tertiary diabetic center in Northern Sri Lanka. BMC Res Notes. 2019;12(1):210.
17. Cho NH, Ahn CW, Park JY, et al. Prevalence of erectile dysfunction in Korean men with type 2 diabetes mellitus. Diabet Med J Br Diabet Assoc. 2006;23(2):198–203.
18. El Saghier EO, Shebl SE, Fawzy OA, et al. Androgen deficiency and erectile dysfunction in patients with type 2 diabetes. Clin Med Insights Endocrinol Diabetes. 2015;8:55–62.
19. Betancourt-Albrecht M, Cunningham GR. Hypogonadism and diabetes. Int J Impot Res. 2003;15(S4):S14–20.

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