Objective — To assess associations of sex hormones with impaired fasting glucose (IFG) and type 2 diabetes in men.

Research Design and Methods — A total of 3,156 African American, Non-Hispanic white, Hispanic, and Chinese-American men aged 45–84 years who participated in the baseline visit of the Multi-Ethnic Study of Atherosclerosis (MESA) were included. Odds ratios and 95% CIs for type 2 diabetes and IFG compared with normal fasting glucose for quartiles of hormones were estimated.

Results — After adjusting for age, ethnicity, BMI, and waist circumference, IFG and diabetes were associated inversely with total testosterone and sex hormone–binding globulin (SHBG) and positively with estradiol (E2). Dehydroepiandrosterone was positively associated with IFG but not with diabetes. Associations did not differ across ethnic groups.

Conclusions — Regardless of obesity, total testosterone and SHBG were associated inversely and E2 was associated positively with IFG and diabetes in men. Further research is warranted to better understand the underlying biological mechanisms.

Sex hormones have been associated with type 2 diabetes in men (1,2). Some studies (1,2) have shown that these associations were independent of obesity. In the Third National Health and Nutrition Examination Survey (NHANES III) (2), the only study to include a multiethnic sample, power was insufficient to determine whether associations differed by ethnicity. The population-based Multi-Ethnic Study of Atherosclerosis (MESA), initiated in 2000, provides an opportunity to evaluate cross-sectional associations of sex hormones with both type 2 diabetes and impaired fasting glucose (IFG) in men aged 45–84 years while taking into consideration measures of obesity and ethnicity. Similar analyses examining associations in postmenopausal women (3) were conducted separately because previous research has shown that there is a sex dimorphism in hormone associations with type 2 diabetes (1).
Table 1—Association of quartiles of sex hormones with normal fasting glucose, IFG, and type 2 diabetes status: Multi-Ethnic Study of Atherosclerosis (2000–2002)

| Hormone               | Q1 (min–max)   | Q2 (min–max)   | Q3 (min–max)   | Q4 (min–max)   | Q1 (min–max)   | Q2 (min–max)   | Q3 (min–max)   | Q4 (min–max)   | P_trend* |
|-----------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------|
| Testosterone (nmol/l) | 8.90 (0.03–11.35) | 12.81 (11.38–14.23) | 15.87 (14.26–17.77) | 22.05 (17.80–68.36) | 8.90 (0.03–11.35) | 12.81 (11.38–14.23) | 15.87 (14.26–17.77) | 22.05 (17.80–68.36) | 0.0054   |
| Chinese               | 0.88 (0.33–1.27)  | 1.07 (0.67–1.71)  | 1.26 (1.07–2.14)  | 1.50 (1.26–2.78)  | 0.86 (0.33–1.27)  | 1.07 (0.67–1.71)  | 1.26 (1.07–2.14)  | 1.50 (1.26–2.78)  | 0.14      |
| Non-Hispanic white   | 0.86 (0.68–1.08)  | 1.05 (0.76–1.61)  | 1.26 (0.96–2.42)  | 1.50 (1.26–2.78)  | 0.86 (0.68–1.08)  | 1.05 (0.76–1.61)  | 1.26 (0.96–2.42)  | 1.50 (1.26–2.78)  | 0.0002   |
| SHBG (nmol/l)        | 25.3 (8.6–31.8)   | 36.1 (23.5–40.8) | 46.4 (39.0–52.7) | 70.1 (52.8–108.9) | 25.3 (8.6–31.8)   | 36.1 (23.5–40.8) | 46.4 (39.0–52.7) | 70.1 (52.8–108.9) | 0.0001   |
| E2 (pmol/l)          | 67.4 (29.4–84.4)  | 99.4 (88.1–110.1) | 125.4 (113.8–139.5) | 178.2 (143.2–661.8) | 67.4 (29.4–84.4)  | 99.4 (88.1–110.1) | 125.4 (113.8–139.5) | 178.2 (143.2–661.8) | 0.005    |
| Chinese               | 0.91 (0.35–1.56)  | 1.04 (0.35–1.56)  | 1.04 (0.35–1.56)  | 1.04 (0.35–1.56)  | 0.91 (0.35–1.56)  | 1.04 (0.35–1.56)  | 1.04 (0.35–1.56)  | 1.04 (0.35–1.56)  | 0.81      |
| Non-Hispanic white   | 0.91 (0.35–1.56)  | 1.04 (0.35–1.56)  | 1.04 (0.35–1.56)  | 1.04 (0.35–1.56)  | 0.91 (0.35–1.56)  | 1.04 (0.35–1.56)  | 1.04 (0.35–1.56)  | 1.04 (0.35–1.56)  | 0.81      |
| Dehydroepiandrosterone (nmol/l) | 7.1 (0.9–9.1) | 10.2 (8.4–12.0) | 13.3 (11.8–16.9) | 21.4 (17.8–49.1) | 7.1 (0.9–9.1) | 10.2 (8.4–12.0) | 13.3 (11.8–16.9) | 21.4 (17.8–49.1) | 0.0055   |

Data are OR (95% CI) unless otherwise indicated. ORs are adjusted for age, BMI, waist circumference, and in the pooled analysis, ethnicity. IFG: 100 mg/dl fasting glucose; type 2 diabetes: fasting glucose ≥126 mg/dl or current use of diabetes medication. *P-value from a model treating hormone as a continuous variable. Q, quartile.
RESULTS — The prevalence of IFG and diabetes was 30 and 21% in African Americans, 32 and 9% in non-Hispanic whites, 35 and 20% in Hispanics, and 40 and 15% in Chinese, respectively.

Interactions between ethnicity and hormones for diabetes or IFG were not statistically significant when using quartiles of sex hormones (P > 0.28) or continuous hormone variables (P > 0.19). Because this may be a consequence of limited power, analyses are presented by ethnicity and also pooled (Table 1). For total testosterone, the ORs for the highest quartile compared with those for the lowest ranged from 0.26 to 0.77 for diabetes and from 0.50 to 0.85 for IFG. Similarly, all ORs for the highest quartile of sex hormone–binding globulin (SHBG) were <1.0 for diabetes and IFG. In contrast, ORs for estradiol (E2), especially in Chinese men, indicated positive associations with IFG and diabetes.

In the pooled analysis, the inverse associations of total testosterone and SHBG, and the positive association of E2, with type 2 diabetes were strong. SHBG was significantly but not linearly associated with IFG. Dehydroepiandrosterone was positively associated with IFG but not with diabetes. Adjustment for other confounders did not attenuate these associations (data not shown).

CONCLUSIONS — Despite adjustment for BMI and waist circumference, in analyses pooling ethnicities, we observed significant inverse associations of total testosterone and SHBG with diabetes and IFG, whereas E2 was positively associated. Our findings are consistent with the results of a meta-analysis. NHANES III results for BMI and waist circumference, in diabetes. Adjustment for other confounders did not attenuate these associations (data not shown).

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