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Type 2 diabetes mellitus and testosterone: a meta-analysis study. I

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Abstract: Several studies suggest that type 2 diabetes mellitus (T2DM) is often associated with male hypogonadism. Despite the well-known link, the role of testosterone replacement therapy (TRT) in T2DM has not been completely clarified. The aim of the present study was to analyse systematically the relationship between androgen levels and T2DM by reviewing and meta-analysing available prospective and cross-sectional studies. In addition, a specific meta-analysis on the metabolic effects of TRT in available randomized clinical trials (RCTs) was performed. An extensive Medline search was performed including the following words: 'testosterone', 'type 2 diabetes mellitus' and 'males'. Of 742 retrieved articles, 37 were included in the study. In particular 28, 5 and 3 were cross-sectional, longitudinal and interventional studies, respectively. A further unpublished RCT was retrieved from <http://www.clinicaltrials.gov>. T2DM patients showed significantly lower testosterone plasma levels in comparison with non-diabetic individuals. Similar results were obtained when T2DM subjects with and without erectile dysfunction were analysed separately. Meta-regression analysis demonstrated that ageing reduced, while obesity increased, these differences. However, in a multiple regression model, after adjusting for age and body mass index (BMI), T2DM was still associated with lower total testosterone (TT) levels (adjusted $r = -0.568$; $p < 0.0001$). Analysis of longitudinal studies demonstrated that baseline TT was significantly lower among patients with incident diabetes in comparison with controls (HR = $-2.08[-3.57;-0.59]$; $p < 0.001$). Combining the results of RCTs, TRT was associated with a significant reduction in fasting plasma glucose, HbA1c, fat mass and triglycerides. Conversely, no significant difference was observed for total and high-density lipoprotein cholesterol, blood pressure and BMI. The meta-analysis of the available cross-sectional data suggests that T2DM can be considered independently associated with male hypogonadism. Although only few RCTs have been reported, TRT seems to improve glycometabolic control as well as fat mass in T2DM subjects