Gender-affirming Hormone Therapy and Risk of Diabetes in Transgender Persons

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Most transgender people request gender-affirming hormone therapy (GAHT) to affirm their gender identity and to improve quality of life and well-being (1). GAHT has been regarded as safe when following guidelines to ensure that sex hormone concentrations do not exceed values found in men and women (1). However, recent large cohort studies have raised concerns about the long-term risk of cardiovascular disease after receipt of GAHT (2, 3). Transgender women followed at the Amsterdam Cohort of Gender Dysphoria experienced higher than expected cardiovascular deaths compared to the general Dutch population (2). In the US-based STRONG cohort, transgender women had increased rates of stroke compared with cisgender men and women (3). The reasons for the increased rates of major cardiovascular events (MACEs) found in transgender women are unclear. Increased risk of diabetes may contribute to the increased risk of MACEs associated with GAHT. Early studies have suggested that GAHT worsens insulin resistance and risk of diabetes in transgender women (4). In addition, GAHT in transgender women has been associated with increased body mass index, which may further increase the risk of diabetes (5).

Investigators from the Amsterdam Cohort of Gender Dysphoria investigated whether receipt of GAHT was associated with risk of diabetes (6). They included transgender people receiving GAHT and who had at least 1 follow-up visit to the clinic. They used data from the National Civil Record Registry as a reference group to calculate the rate of type 2 diabetes in the general Dutch population. Diabetes was defined in both groups as receipt of medication for treatment of type 2 diabetes. The transgender population consisted of 2585 transgender women and 1514 transgender men with a median follow-up period of 30 and 23 years, respectively. During the study period, 90 and 32 transgender women and men developed diabetes with a median age at diagnosis of 55 and 50 years, respectively. Compared with the general Dutch population, the standardized incidence ratio for diabetes was not elevated in transgender men or women.

A similar study examined the risk of diabetes in transgender people in the United States (7). In the STRONG cohort, diabetes was defined using the SUPREME-DM criteria, a standardized definition for diabetes developed for use in electronic medical records research. To be classified as having diabetes, participants had laboratory evidence of diabetes (2 or more of the following criteria hemoglobin A1c ≥ 6.5%, fasting glucose ≥126 mg/dL, random glucose values ≥200 mg/dL), receipt of diabetes medication, or an inpatient or outpatient diagnosis code indicating diabetes. The investigators did not find differences in baseline prevalence or incidence of diabetes in transgender women following initiation of GAHT compared with reference cisgender male and female controls. However, when examining the baseline prevalence and incidence of diabetes in transgender women both taking and not taking GAHT, there was an increased incidence and prevalence of diabetes compared with cisgender women, suggesting the risks of diabetes may not be related to GAHT.

Smaller prospective studies have suggested that GAHT may negatively influence markers of insulin resistance and glucose metabolism in transgender women. However, these subtle changes in insulin resistance and glucose metabolism are in contrast to these 2 cohort studies. If GAHT does not increase risk of diabetes, it remains unanswered why there appears to be increased risk of MACE in transgender women. Transgender women may face gender minority stress that may, in turn, increase psychologic stress and behaviors (smoking, alcohol misuse, poor diet, decreased physical activity) associated with MACE (8). Also, transgender people might have less access to preventive health care; thus, screening and treatment for diabetes is delayed compared with the cisgender population. Until more prospective studies are conducted, screening and treatment of cardiovascular disease in transgender people should follow established guidelines for cisgender populations. More data are required to determine if earlier screening and/or more than routine screening is required for diabetes, especially in transgender women.

Conflict of Interest

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**Data Availability**

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

**References**


