

Cardiac autonomic neuropathy, the difference weighs on menopause

Aims: Sexual differences manifest in cardiovascular outcomes among individuals with type 1 diabetes. Data on the relationship between sex and cardiac autonomic neuropathy (CAN) in these patients are limited and subject to controversy. The objective of this study was to investigate gender-related variations in the prevalence of CAN in type 1 diabetes and explore their connections with sex steroids.

Methods: A cross-sectional study, including 322 consecutively patients with type 1 diabetes, was conducted. CAN was performed using Ewing's score and power spectral heart rate data. The Authors assessed the following sex hormones by liquid chromatography/tandem mass spectrometry: total testosterone (T), sex hormone-binding globulin (SHBG), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and oestradiol (E₂) in serum samples.

Results: When considering the entire study cohort, the prevalence of CAN did not exhibit a significant difference between women and men. Considering the age parameter, the prevalence of CAN was comparable among young men and those over 50 years. However, among women over 50 years, the prevalence of CAN doubled that of their younger counterparts [45.8% (32.6; 59.7) vs. 20.4% (13.7; 29.2), respectively]. CAN was categorized as early/mild in 38 cases [79% (66; 88)] and definite in 10 [21% (12; 34)] in women, whereas in men these findings were definite in only 2 cases [4% (1; 15)] (P=0.020). The odds ratio (OR) for CAN was 3.3 times higher in women over 50 years compared to younger women. Additionally, women displayed a more severe form of CAN than men. Peri- and menopausal women had an OR of 3.5 (1.7; 7.2) for developing CAN compared to their reproductive-aged counterparts [CAN prevalence: 51% (37; 65) vs. 23% (16; 32), respectively]. Women with CAN had higher total T/E₂ and free T/E₂ molar ratios, lower E₂, and free E₂, compared with those without CAN. CAN was also linked to an increased testosterone/oestradiol ratio in women but to decreased testosterone concentrations in men.

Conclusions: Menopause in women with type 1 diabetes is associated with a rise in the prevalence of CAN. This age-related heightened risk of cardiac autonomic dysfunction is not evident in men. Men and women with type 1 diabetes exhibit divergent associations between circulating androgens and parameters of autonomic function.

Comments. This study highlights the presence of sex differences in the prevalence of CAN in type 1 diabetes. Menopause in women leads to a dramatic increase in the prevalence of CAN compared to women in reproductive age. Women affected by CAN demonstrated lower E₂ and free E₂ concentrations, along with higher T/E₂ ratios, in contrast to female patients without CAN. Estrogens are likely the key hormones involved, modulating para-sympathetic autonomic imbalance (Souza HC and Tezini GC. *Aging Dis.* 2013;4:320-8). This excess risk of CAN might contribute to explain the marked increase in the incidence of cardiovascular disease in the menopausal transition. These results could suggest considering the crucial differences between men and women in a study design process and in the interpretation of the data, especially in the field of autonomic nervous system dysfunctions.

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Reference. Nattero-Chávez L, Insenser M, Quintero Tobar A, Fernández-Durán E, Dorado Avendaño B, Fiers T, Kaufman JM, Luque-Ramírez M, Escobar-Morreale HF. Sex differences and sex steroids influence on the presentation and severity of cardiovascular autonomic neuropathy of patients with type 1 diabetes. *Cardiovasc Diabetol.* 2023 Feb 15;22(1):32. doi: 10.1186/s12933-023-01766-y. PMID: 36793089; PMCID: PMC10127589.

<https://cardiab.biomedcentral.com/articles/10.1186/s12933-023-01766-y>