SEX HORMONES IN MORTALITY AND OTHER ADVERSE HEALTH OUTCOMES AMONG ADULTS UNDERGOING HEMODIALYSIS – A PROSPECTIVE STUDY

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Introduction: Patients with kidney failure on hemodialysis (HD) develop low testosterone (T) and estradiol (E2) profile over time in males and females, respectively. Although low T and E2 are linked to an increased risk of adverse clinical outcomes, it is still unclear if the relationships are modified by diabetes status in patients undergoing HD. We aimed to determine whether endogenous T and E2 levels are associated with all-cause mortality, cardiovascular (CV) events, declining functional status, and quality of life among patients undergoing HD. Furthermore, we aimed to determine whether diabetes would modify any possible relationships.

Methods: A prospective study was conducted in 876 participants of the Canadian Kidney Disease Cohort Study not using exogenous sex hormones (n = 557 males; n = 319 females). Cox proportional hazards models were used to examine the associations between endogenous T in males and E2 in females with all-cause mortality as well as fatal and non-fatal CV events. Adjusted mixed models were used to fit the Health Utility Index (HUI3), and the KDQOL-12 physical and mental component score, where participants were modelled as random effects and visit as a fixed effect.

Results: Median age was 63 (53, 73) years (males) and 67 (61, 76) years (females). 45% of males and 55% of females had diabetes. Over the study period of almost 14 years, 500 (57%) participants died, of which 176 (35%) were CV-related. Compared to middle T tertiles, highest T tertiles were not significantly associated with the risk of all-cause (HR=1.02, [0.76; 1.38]), CV mortality (HR = 1.40, [0.86; 2.28]), having a CV event (HR = 1.18, [0.70; 2.00]), or KDQOL12-MCS (MD = -0.48, [-2.76; 1.80]), but was associated with higher HUI3 scores (mean difference (MD) = 0.06, [0.01; 0.11]) and KDQOL-12 PCS (MD = 2.36, [0.38; 4.34]). Compared to middle E2 tertiles, lowest E2 tertiles were associated with lower risk of all-cause mortality (HR = 0.64, [0.45; 0.92]), but not with CV mortality (HR = 0.69, [0.36; 1.35]), having a CV event (HR = 1.04, [0.49; 2.20]), HUI3 scores (MD = 0.02, [-0.04; 0.07]), KDQOL12-PCS (MD = -1.03, [-3.67; 1.62]), and KDQOL12-MCS (MD = -2.21, [-5.29; 0.88]). However, the highest E2 tertile was associated with lower KDQOL12-PCS (MD = -3.01, [-5.64; -0.39]). Diabetes status did not significantly modify the associations between hormone levels and clinical outcomes.

Conclusion: Higher E2 profile among females undergoing HD was associated with lower quality of life. Whereas in males, higher T profile was linked to higher functional scores and quality of life. These relationships were not modified by diabetes status. Low T in males and high E2 in females may be modifiable risk factors for adverse clinical outcomes, functional status, and quality of life. However, further studies are warranted to assess whether the observed associations were causal.

Key words: Testosterone, Estradiol, Hemodialysis, Type 2 Diabetes, Kidney failure