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Role of Chronotype on Vascular Insulin Sensitivity in Adults with Obesity

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Endothelial function lowers cardiovascular disease risk. Chronotype has a circadian rhythmicity that may regulate and increase endothelial function throughout the day. However, no study has examined insulin action on endothelial function. **PURPOSE** We hypothesized that morning chronotype (MC) would have reduced vascular insulin sensitivity compared to intermediate type (IC). **METHODS** Adults with obesity were classified as either MC (n=24, 20F, MEQ=63.8±0.9, 54.3±1.4yrs, 33.8±0.7kg/m², 24.1±0.9ml/kg/min) or IC (n=26, 21F, MEQ=48.9±1.5, 55.4±1.6yrs, 37.5±1.1kg/m², 21.8±0.7ml/kg/min) per Morningness-Eveningness Questionnaire (MEQ). A 120min euglycemic-hyperinsulinemic clamp (40mU/m²/min, 90mg/dL) was used in the morning to examine vascular insulin sensitivity via brachial artery flow-mediated dilation (%FMD, conduit artery) and post-ischemic flow velocity (PIFV, resistance arteriole). Blood pressure (BP), blood flow (BF), vascular resistance and shear stress at 0 and 120min of the clamp were calculated. Fasting plasma arginine and citrulline, as well as fasting and clamp-derived plasma nitrate/nitrite and ET-1, were assessed as surrogates of nitric oxide and constriction, respectively. Aerobic fitness (VO₂max) and body composition (DXA) were also determined. **RESULTS** IC had higher BMI ($P<0.01$) but lower VO₂max ($P=0.05$). Fasting FMD corrected to shear stress, PIFV, BF, and shear stress were higher, while vascular resistance was lower, in IC than MC (group effect, all $P<0.01$). In response to insulin, both IC and MC decreased FMD corrected to shear stress (time effect, $P=0.003$) and ET-1 (trend time effect, $P=0.09$), with a delayed time to peak (time effect, $P<0.001$). Insulin lowered vascular resistance and raised PIFV, shear rate, BF and heart rate (HR) similarly between groups (time effect, all $P\leq 0.05$). IC had lower fasting and clamp nitrate (group effect, $P=0.003$) and fasting arginine ($P=0.08$). Higher MEQ correlated with lower PIFV ($r=-0.36$, $P=0.02$), shear rate ($r=-0.38$, $P=0.02$), and SBP ($r=-0.38$, $P=0.01$) during the clamp. **CONCLUSION** Although IC had favorable endothelial function compared with MC, both groups responded similarly to insulin. These data suggest that chronotype may influence diurnal variation of endothelial function independent of insulin.

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