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**Cardiovascular Health Effects of Pod-Based Electronic Cigarettes**

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**Objectives:** Robust evidence links combustible cigarette use to chronic cardiovascular disease potentially mediated by endothelial toxicity. Pod-based electronic cigarettes such as JUUL are particularly popular in young adults and deliver high levels of nicotine.

**Methods and Results:** We measured several axes of cardiovascular health and urinary volatile organic compounds (VOCs) in 133 healthy adults (age 18-45) including pod-based electronic cigarette users, combustible cigarette users before and after a structured product use session. Pod-based electronic cigarette use led to increases in systolic blood pressure (6±8mmHg P=0.00001 vs non-use) and heart rate (4.4±7bpm, P=0.00001) to a similar degree as combustible cigarette use (P=NS). Similarly, we observed reductions in vasodilator function measured by brachial artery flow-mediated dilation (-3.2%±2.7%) and heart rate variability (SDNN -5.9±3.3ms) with by pod-based electronic cigarette use to a greater degree than non-use (P<0.001) and similar to combustible cigarette use (P=NS). The effects of pod-based electronic cigarettes persisted in models adjusted for age, race, and sex. The vascular effects were similar across groups of pod-based users including JUUL compared to non-JUUL pods, dual compared to sole electronic cigarette use, never combustible cigarette users compared to former, and across the flavor categories. Urinary cotinine and nicotine levels were higher in cigarette and pod-based users following acute exposure. The product use induced changes in blood pressure, heart rate variability and flow-mediated dilation but not heart rate related to the urinary levels of acrolein metabolites. In endothelial cells isolated from pod-based electronic cigarette users, we observed impaired activation of endothelial nitric oxide synthase suggesting a potential cellular based mechanisms for the observed differences in vasodilator function. Consistent with the human findings, several pod-based electronic cigarette liquids impaired stimulated nitric oxide bioavailability.

**Conclusions:** Our results indicate that pod-based electronic cigarette use decreases endothelial function, raises blood pressure, and reduces heart rate variability to a degree comparable to the use of combustible cigarettes. The acute impact is present in young adults who have never used combustible cigarettes. Exposure to selected metabolites of key harmful elements including acrolein may relate to vascular toxicity. At the level of the endothelial cells, there is impaired nitric oxide activation relevant to the observed impact on vasodilator function. Overall our findings suggest that pod-based electronic cigarette use has adverse cardiovascular impact in healthy young adults. Further studies are ongoing to evaluate the longitudinal impact of electronic cigarette use on vascular health.

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