CORRESPONDENCE



Simple Strategies to Reduce Cardiac Strain in Older Adults in Extreme Heat

TO THE EDITOR: Heat-related adverse effects on health are increasingly common with climate change. Older adults are disproportionately affected, especially those with heart disease, owing to heat-induced increases in cardiac strain. Air conditioning is protective, but many persons with low income lack access.

Electric fans and skin wetting are simple, low-cost cooling approaches for persons without access to air conditioning,⁴ but the efficacy of these approaches is unproven in heat-vulnerable groups. The Centers for Disease Control and Prevention states that fans can worsen heat stress at temperatures greater than 32.2°C (90.0°F).⁵ We assessed the effects of fan use, skin wetting, or both on heat-induced cardiac strain in older adults with coronary artery disease and older adults without coronary artery disease during exposure to high temperatures with a high or low relative humidity.

We conducted randomized crossover studies at the University of Sydney and the Montreal Heart Institute. Participants were exposed to two hot environments and completed up to eight exposures, each separated by more than 72 hours. Participants sat for 3 hours in an environment with a mean (±SD) temperature of 38.0±0.1°C and a mean relative humidity of 60±1% (hot and

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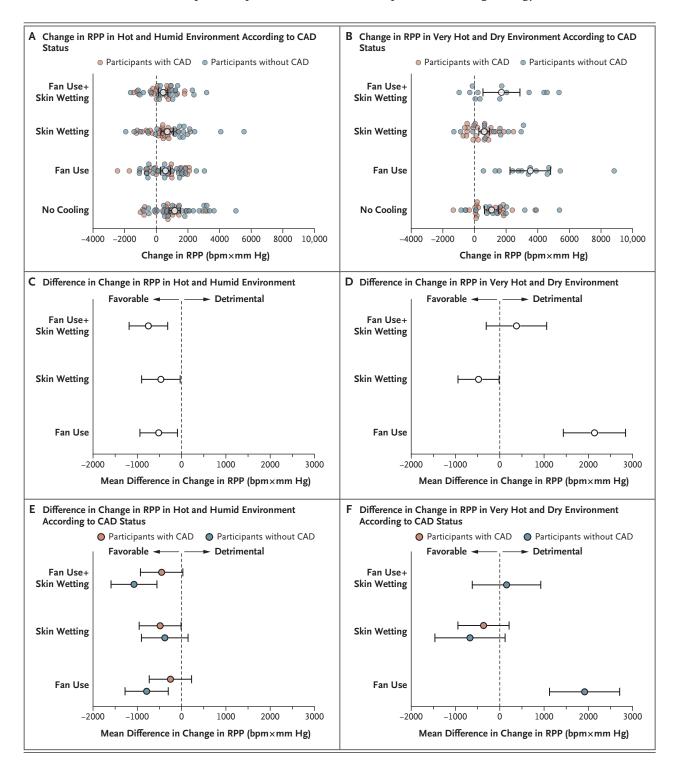
humid) or an environment with a mean temperature of 45.0±0.1°C and a mean relative humidity of 15±1% (very hot and dry). Fan use, skin wetting, fan use plus skin wetting, and no cooling (control) were assessed in both environments in participants without coronary artery disease and in the hot and humid environment in patients with

Figure 1 (facing page). Effect of Cooling Strategies on Heat-Related Cardiac Strain.

Shown are changes from baseline in the rate-pressure product (RPP) with no cooling (control), fan use, skin wetting, and fan use plus skin wetting after exposure for 3 hours to a hot and humid environment (Panel A) or a very hot and dry environment (Panel B) in participants with coronary artery disease (CAD) and those without coronary artery disease. The RPP is calculated as the heart rate in beats per minute (bpm) multiplied by the systolic blood pressure in millimeters of mercury. The hot and humid environment had a temperature of 38.0°C and a relative humidity of 60%. The very hot and dry environment had a temperature of 45.0°C and a relative humidity of 15%. Also shown are mean differences from control in the change from baseline in the RPP with each cooling strategy during exposure for 3 hours to the hot and humid environment (Panel C) or the very hot and dry environment (Panel D) in the overall trial population. Panels in the bottom row show mean differences from control in the change from baseline in the RPP with each cooling strategy during exposure for 3 hours to the hot and humid environment (Panel E) or the very hot and dry environment (Panel F) among participants with coronary artery disease and those without coronary artery disease. The change from baseline in the RPP during exposure to the very hot and dry environment was not assessed for cooling strategies involving fan use in adults with coronary artery disease, owing to safety concerns. I bars indicate 95% confidence intervals (Panels A, B, and D through F) or 98.33% confidence intervals (Panel C). The 95% confidence intervals were not adjusted for multiplicity and should not be used in place of hypothesis testing.

coronary artery disease. Skin wetting and no cool- (the heart rate in beats per minute [bpm] multi-

ing were assessed in the very hot and dry environ- plied by the systolic blood pressure in millimeters ment in participants with coronary artery disease. of mercury). In a prespecified analysis, we used The primary outcome was the change from linear mixed models combining data from the baseline to hour 3 in the rate-pressure product two sites to compare each cooling strategy with



control, in both the hot and humid environment and the very hot and dry environment, with regard to the primary outcome. Additional details about the trial methods, participant characteristics, and representativeness of the participants are provided in the Supplementary Appendix (available with the full text of this letter at NEJM.org, along with the protocol and statistical analysis plan).

We assessed 31 adults without coronary artery disease (mean age, 70 years; 17 women) at the University of Sydney and 27 adults with coronary artery disease (mean age, 66 years; 2 women) at the Montreal Heart Institute. The rate-pressure product increased during exposure to the hot and humid environment and the very hot and dry environment with each cooling approach and no cooling (Fig. 1A and 1B). After exposure to the hot and humid environment for 3 hours, heat-induced increases from baseline in the rate-pressure product were reduced by fan use (mean difference in change vs. control, -517 bpm×mm Hg; 98.33% confidence interval [CI], -941 to -93; P=0.004), skin wetting (mean difference in change vs. control, -468 bpm×mm Hg; 98.33% CI, -903 to -32; P=0.01), and fan use plus skin wetting (mean difference in change vs. control, -750 bpm×mm Hg; 98.33% CI, -1185 to -314; P<0.001) (Fig. 1C).

The assessment of fan use during exposure to the very hot and dry environment was halted after 14 persons (all without coronary artery disease) had participated. The decision to end this assessment was made because the increase in the rate-pressure product from baseline to the end of the exposure was 3 times as high with fan use as with control (3223 vs. 1084 bpm × mm Hg; mean difference in change, 2139 bpm×mm Hg; 95% CI, 1437 to 2842) (Fig. 1D) and because 43% of the persons (6 of 14) who used fans after entering the very hot and dry environment withdrew before 3 hours because they felt unwell (in 2 participants), had a high heart rate that met the trial criteria for withdrawal (in 3 participants), or had abnormal findings on electrocardiography (in 1 participant) (Table S5). In contrast, heat-induced increases from baseline in the rate-pressure product during exposure to the very hot and dry environment were reduced by skin wetting (mean difference in change vs. control, -478 bpm×mm

Hg; 95% CI, -943 to -13) (Fig. 1D). Results appeared to be broadly similar in participants with coronary artery disease and those without coronary artery disease (Fig. 1E and 1F). Comparisons of the cooling strategies with control in each environment, stratified according to beta-blocker use, sex, and season, are provided in Tables S6 and S7.

The findings from our trial support the benefit of fan use, skin wetting, or both for reducing heat-induced cardiac strain in older adults with coronary artery disease and older adults without coronary artery disease in environments with temperatures of up to 38°C with high relative humidity. In a very hot and dry environment, as defined by a temperature of 45°C with a relative humidity of 15%, our results showed a harm with fan use and a benefit with skin wetting. Our results may not be generalizable to exposures longer than 3 hours or to persons with unmanaged coronary artery disease or with other coexisting conditions. Potential barriers to the use of these cooling strategies warrant assessment in field studies.

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Raw data used for the analyses reported in this letter are freely available on request by contacting the corresponding authors.

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Semaglutide for Chronic Kidney Disease in Type 2 Diabetes

TO THE EDITOR: In the FLOW (Evaluate Renal Function with Semaglutide Once Weekly) trial, Perkovic et al. (July 11 issue)¹ explored the effect of semaglutide on kidney disease outcomes in patients with type 2 diabetes. Although the trial provides valuable insights, several methodologic limitations should be noted.

Although the trial had adequate statistical power for the analysis of the primary outcome, it did not include the use of sodium—glucose cotransporter 2 (SGLT2 inhibitors), mineralocorticoid-receptor antagonists (MRAs), and other established therapies in the trial cohort. Issues with adherence and a notable rate of discontinuation among the participants could affect interpretation of the treatment effect. In addition, the limited representation of patients from diverse racial and ethnic backgrounds may restrict the generalizability of findings to broader populations. Furthermore, the lack of blinding for the assessment of certain adverse events may introduce bias in safety assessments.

Overall, although the trial highlights the potential benefits of semaglutide, these methodologic limitations underscore the complexity of interpreting its real-world implications. The au-

thors rightly advocate for rigorous methods and cautious interpretation and emphasize the need for further research to clarify the role of semaglutide in managing chronic kidney disease across diverse demographic groups.

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No potential conflict of interest relevant to this letter was reported.

1. Perkovic V, Tuttle KR, Rossing P, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. N Engl J Med 2024;391:109-21.

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THE AUTHORS REPLY: Passos et al. state that SGLT2 inhibitors were not used in our trial, but as noted in our article, 15.6% of the participants were receiving these agents at trial entry, and a similar percentage started receiving them during follow-up. It is important to note that recruitment of participants began in 2019, before the widespread use of SGLT2 inhibitors and MRAs in this population. Although