also be inferred from the mortality benefit and rapid clinical improvement in patients with several forms of immunosuppression following convalescent plasma transfusion.1 These positive safety data are promising, given that immunocompromised patients will continue to represent a vulnerable population throughout the duration of the COVID-19 pandemic and may be among those medically advised to not receive vaccination or unable to mount a robust humoral response to vaccination.3

Given the link between COVID-19 and thromboembolic diseases and plasma serving as a source of both procoagulant and anticoagulant factors, there may be lingering concerns that convalescent plasma escalates thromboembolic risk, especially among severely ill patients.8 At present, the aggregate epidemiologic data suggest that convalescent plasma does not increase the thromboembolic risk in patients with COVID-19. To support and confirm these findings, future experimental studies should assess the impact of convalescent plasma on a panel of coagulation factors in patients with COVID-19 or evaluate whether the coagulation profile of COVID-19 convalescent plasma poses a greater thromboembolic risk than standard fresh frozen plasma.

The importance of the work by Franchini and Cruciani is that they have broadly shown there is a consistent safety profile for the use of human convalescent plasma in the treatment of COVID-19. Whereas there are mixed interpretations on the effectiveness of convalescent plasma, the lack of safety concerns must be carefully weighed in the context of the potential for benefit the treatment may offer during the remainder of the COVID-19 pandemic.

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Effects of Empagliflozin Treatment on Cardiac Biomarkers in Adults With Metabolically Healthy Obesity: Results From a Randomized, Placebo-Controlled Clinical Trial

To the Editor: High-sensitivity cardiac troponin T (hs-cTnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are biomarkers that reflect myocardial injury and cardiac strain, respectively. Subclinical elevations in these routinely assayed biomarkers are associated with increased risk of incident heart failure (HF) in population-based cohorts and have been proposed for prevention of HF (eg, sodium glucose cotransporter 2 inhibitors [SGLT2i] in diabetes).3 However, studies of the safety and treatment effects of SGLT2i on cardiac biomarkers in adults who have metabolically healthy obesity (without diabetes or other major cardiorenal comorbidities) are lacking. Therefore, we sought to examine the safety of short-term administration of the SGLT2i and effects on hs-cTnT and NT-proBNP in adults with metabolically healthy obesity.

In this single-center randomized, placebo-controlled trial, adults aged 18 years and older with obesity (body mass index ≥30 kg/m²) and without diabetes (baseline hemoglobin A1c level <6.5%), HF, or chronic kidney disease were randomized to empagliflozin 10 mg daily or placebo for 3
Details of the study design have been published previously (NCT02833415), and no stratification factors were used in randomization.2 Briefly, the cardiac biomarkers hs-cTnT and NT-proBNP (Cobas 8000, Roche Diagnostics) were assessed at baseline and the final study visit. Levels of hs-cTnT below the limit of detection were set to 3.0 ng/L (to convert hs-cTnT values to μg/L, multiply by 0.001). For the primary analysis, biomarkers were analyzed within-group with paired baseline to follow-up testing using an intention-to-treat analysis. Pairwise characteristics were compared using Wilcoxon rank sum tests. All participants provided written informed consent, and the protocol was approved by the Institutional Review Board at the University of Texas Southwestern Medical Center.

Of the 35 participants who completed the study, 18 were randomized to empagliflozin 10 mg daily and 17 to the placebo group (mean drug adherence, 94%). Median (interquartile range [IQR]) age was 53 (46 to 59) years; the cohort was 63% female, and 34% self-identified as Black (Table). Median (IQR) body mass index of the group was 35 (33 to 40) kg/m². At baseline, most participants had hs-cTnT concentration below the minimum level of detection; 23% had an elevated level of 6 ng/L or higher, and 9% had an abnormal level of 14 ng/L or higher. There were no significant changes in hs-cTnT or NT-proBNP levels between baseline and 3-month follow-up in patients randomized to either arm in the study.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N=35)</th>
<th>Empagliflozin (n=18)</th>
<th>Placebo (n=17)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>53 (46-59)</td>
<td>50.5 (43-56)</td>
<td>54.0 (48-59.0)</td>
<td>.40</td>
</tr>
<tr>
<td>Female</td>
<td>22.2 (62.9)</td>
<td>11 (61.1)</td>
<td>11 (64.7)</td>
<td>.83</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td>.50</td>
</tr>
<tr>
<td>Black</td>
<td>12 (34.3)</td>
<td>5 (27.8)</td>
<td>7 (41.2)</td>
<td>.40</td>
</tr>
<tr>
<td>White</td>
<td>20 (57.1)</td>
<td>11 (61.1)</td>
<td>9 (52.9)</td>
<td>.35</td>
</tr>
<tr>
<td>Other</td>
<td>3 (8.6)</td>
<td>2 (11.1)</td>
<td>1 (5.9)</td>
<td>.81</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>130 (120-139)</td>
<td>126 (117-138)</td>
<td>132 (127-141)</td>
<td>.18</td>
</tr>
<tr>
<td>Hemoglobin A1c (%)</td>
<td>5.8 (5.4-6.0)</td>
<td>5.6 (5.4-5.9)</td>
<td>5.9 (5.6-6.1)</td>
<td>.09</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>35 (33-40)</td>
<td>37 (33-39)</td>
<td>35 (33-40)</td>
<td>.96</td>
</tr>
<tr>
<td>Total body fat (%)</td>
<td>45 (36-50)</td>
<td>46 (34-49)</td>
<td>45 (38-53)</td>
<td>.35</td>
</tr>
<tr>
<td>Total body lean mass (%)</td>
<td>25 (21-29)</td>
<td>24 (22-30)</td>
<td>25 (21-28)</td>
<td>.36</td>
</tr>
<tr>
<td>Visceral fat (kg)</td>
<td>5.4 (3.9-7.2)</td>
<td>5.4 (4.0-7.3)</td>
<td>4.3 (3.8-6.7)</td>
<td>.81</td>
</tr>
<tr>
<td>High visceral fata,e</td>
<td>17 (5.15)</td>
<td>10 (62.5)</td>
<td>7 (41.2)</td>
<td>.30</td>
</tr>
<tr>
<td>hs-cTnT (ng/L)</td>
<td>3.0 (3.0-3.0)</td>
<td>3.0 (3.0-3.0)</td>
<td>3.0 (3.0-3.0)</td>
<td>.75</td>
</tr>
<tr>
<td>Elevated hs-cTnT ≥6 ng/L</td>
<td>8 (22.9)</td>
<td>4 (22.2)</td>
<td>4 (23.5)</td>
<td>.10</td>
</tr>
<tr>
<td>Abnormal hs-cTnT ≥14 ng/L</td>
<td>3 (8.6)</td>
<td>1 (5.6)</td>
<td>2 (11.8)</td>
<td>.60</td>
</tr>
<tr>
<td>Change in hs-cTnT (absolute, ng/L)</td>
<td>0 (0.0-0.3)</td>
<td>0 (0.0-0.4)</td>
<td>0 (0.0-0.2)</td>
<td>.76</td>
</tr>
<tr>
<td>Change in hs-cTnT (relative, %)</td>
<td>0 (0-2.5)</td>
<td>0 (0-6.0)</td>
<td>0 (0-1.5)</td>
<td>.83</td>
</tr>
<tr>
<td>NT-proBNP (pg/mL)</td>
<td>35.1 (21.4-53.7)</td>
<td>29.6 (19.8-42.0)</td>
<td>43.7 (26.5-63.6)</td>
<td>.10</td>
</tr>
<tr>
<td>≥100 pg/mL</td>
<td>3 (8.6)</td>
<td>1 (5.6)</td>
<td>2 (11.8)</td>
<td>.60</td>
</tr>
<tr>
<td>≥75th sex-specific percentile</td>
<td>10 (28.6)</td>
<td>3 (16.7)</td>
<td>7 (41.2)</td>
<td>.15</td>
</tr>
<tr>
<td>Change in NT-proBNP (absolute, pg/mL)</td>
<td>-2.2 (−13.9 to 132)</td>
<td>0.1 (−8.8 to 11.2)</td>
<td>−4.2 (−16.4 to 16.3)</td>
<td>.72</td>
</tr>
<tr>
<td>Change in NT-proBNP (relative, %)</td>
<td>-4.1 (−37.5 to 40.0)</td>
<td>0.4 (−37.3 to 25.7)</td>
<td>−9.8 (−37.5 to 61.4)</td>
<td>1.0</td>
</tr>
<tr>
<td>Cardiometabolic risk level ≥3a,e</td>
<td>10 (32.3)</td>
<td>5 (33.3)</td>
<td>5 (31.3)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

a hs-cTnT, high-sensitivity cardiac troponin T; NT-proBNP, N-terminal pro-B-type natriuretic peptide.
b To convert hs-cTnT values to μg/L, multiply by 0.001; to convert NT-proBNP values to pmol/L, multiply by 0.1182.
c Data are median (interquartile range) or proportion (%) as appropriate.
d High visceral fat is defined as greater than the sex-specific median population value. Cardiometabolic risk level is count of risk factors (fasting glucose concentration ≥100 mg/dL, blood pressure ≥130/85 mm Hg, triglycerides ≥150 mg/dL, waist circumference ≥40 inches in men or ≥35 inches in women).
e For hs-cTnT that is undetectable (<6.0 ng/L), 3.0 ng/L is used. N=31.
In this randomized, placebo-controlled clinical trial, we found that nearly 1 in 10 individuals with metabolically healthy obesity had an elevated hs-cTnT level of 14 ng/L or higher and NT-proBNP level of 100 pg/mL or higher. There were no significant changes in cardiac biomarkers with short-term treatment of empagliflozin in this sample. No adverse effects of hypoglycemia were observed, and the drug was well tolerated. Limitations of this study include the small sample size and relatively short treatment duration. However, these findings are hypothesis generating and support further analyses to investigate risk-based primary prevention of HF with SGLT2i in larger clinical trial populations of individuals with metabolically healthy obesity.

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