Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Figure A and B, treatment with CP did not increase the risk of overall adverse events (RD, 0.01; 95% CI, −0.02 to 0.03; P=.65) and severe adverse events (RD, 0.00; 95% CI, −0.03 to 0.03; P=.81) compared with standard treatment. Similarly, the rate of thromboembolic events did not differ between the study groups (1.4% in the CP arm vs 1.7% in the control arm; RD, 0.00; 95% CI, −0.01 to 0.00; P=.24; Figure C). In addition, the funnel plot of comparison of all 3 outcomes (all, severe, and thromboembolic adverse reactions; Supplemental Figure, available online at http://www.mayoclinicproceedings.org) appeared to be symmetric, suggesting a substantial homogeneity among the included studies and the lack of publication bias.

In conclusion, the results of this updated meta-analysis confirm the safety of CP transfusion and, in particular, document the very low rate (0.7%) of CP transfusion−related serious adverse reactions, similar to that reported in the large US Expanded Access Program.[2] Differing from the previous systematic reviews, we have focused our analysis on the CP-related thromboembolic risk, considering the particular critical setting of COVID-19, with a hyperinflammatory and hypercoagulative state, and the concerns from some clinicians.[3] After a careful analysis of the published literature, we can conclude that the addition of CP to the COVID-19 treatment does not increase the patients' thromboembolic risk. Finally, we personally think that considering the lack of valid anti−COVID-19 therapies, the relatively low costs, and the high safety profile, CP collection and use should be endorsed and implemented by governments of developing and developed countries, without waiting for conclusive evidence of its efficacy.[4]

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

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In Reply—How Safe Is COVID-19 Convalescent Plasma?

To the Editor: We would like to thank Franchini and Cruciani for their letter in response to our systematic review and meta-analysis studying the effect of convalescent plasma therapy on the mortality of patients diagnosed with coronavirus disease 2019 (COVID-19).[1] This letter highlights important new meta-analytical data based on 30 controlled studies (including 14 randomized clinical trials) demonstrating that convalescent plasma transfusion does not increase the risk of adverse events, including thromboembolic events, compared with patients diagnosed with COVID-19 who either were not transfused or were transfused with standard fresh frozen plasma. This new safety analysis supports the viewpoint that human convalescent plasma has a favorable risk-benefit ratio, particularly when it is reviewed in the context of the mosaic of evidence supporting some degree of effectiveness of convalescent plasma therapy for COVID-19.[2] Taken as a whole, these data support the continued use of convalescent plasma as the COVID-19 pandemic endures, especially in regions with limited vaccine access and in immunocompromised patients who cannot mount effective immune responses to vaccines.[3]

At the onset of the COVID-19 pandemic, several theoretical safety risks regarding convalescent plasma therapy were raised, including the potentiation of COVID-19 respiratory deterioration through antibody-dependent enhancement or cytokine storms, transfusion-associated circulatory overload, and enhanced thromboembolic risk.[4] However, the meta-analytical safety data presented in the letter by Franchini and Cruciani along with the consistent signatures of safety emerging from worldwide use of convalescent plasma, including in the United States under the Expanded Access Program and Emergency Use Authorization, have generally allayed these safety concerns.[5,6] Convalescent plasma safety can

also be inferred from the mortality benefit and rapid clinical improvement in patients with several forms of immunosuppression following convalescent plasma transfusion.[7] 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).[1] 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 $\geq$30 kg/m^2) and without diabetes (baseline hemoglobin A_{1c} level <6.5%), HF, or chronic kidney disease were randomized to empagliflozin 10 mg daily or placebo for 3