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REPLY: Pitfalls of Unfractionated Heparin Use During ST-Segment Elevation Myocardial Infarction in Patients With COVID-19 Infection

We appreciate the interest Dr. Martin and colleagues have taken in our recent study "High thrombus burden in patients with COVID-19 presenting with ST-segment elevation myocardial infarction" (1). To respond directly to the questions raised: 1) in all cases, the first dose of unfractionated heparin was administered before wire passage; 2) the first activated clotting time (ACT) was measured 10 to 15 min after this loading dose; 3) baseline ACTs were not routinely measured because all ST-segment elevation myocardial infarction (STEMI) percutaneous coronary intervention (PCI) was done according to usual clinical protocols (baseline assessment of ACT is not standard practice in STEMI PCI); 4) ACTs were measured using the Haemochron instrument (Werfen, Birchwood Park, United Kingdom); as previously shown with this device, glycoprotein IIb/IIIa inhibition prolongs ACT rather than reducing it; thus, increased glycoprotein IIb/IIIa inhibitor use for the COVID-19 group would not explain the findings of lower ACTs (2); and 5) weight-adjusted total heparin doses to maintain therapeutic ACTs were documented in Table 2 of the original publication (1), which demonstrated no significant differences.

Our correlation analysis of weight-adjusted heparin dosing and first ACT measurement was suggestive of heparin resistance among patients with COVID-19 and STEMI, that is, patients with COVID-19 required higher doses of heparin to achieve therapeutic ACTs (Figure 1). Although nonsignificant, we believe these changes are an important signal, and further study is needed. These data were supportive of other small series that suggested heparin resistance among patients with COVID-19 who need intensive care (unfractionated and low-molecular-weight heparin) (3). Therefore, it is likely that use of enoxaparin, despite holding a Class IIa recommendation in current STEMI guidelines, may demonstrate similar findings to unfractionated heparin. Furthermore, the increased risk of stent thrombosis associated with bivalirudin as a heparin alternative in PCI (4) was not ideal in the prothrombotic state associated with COVID-19. Our study demonstrated that a combination of unfractionated heparin and glycoprotein IIb/IIIa inhibition was safe in supporting primary PCI in the COVID-19 cohort, but that regular ACT monitoring to maintain therapeutic levels was needed.

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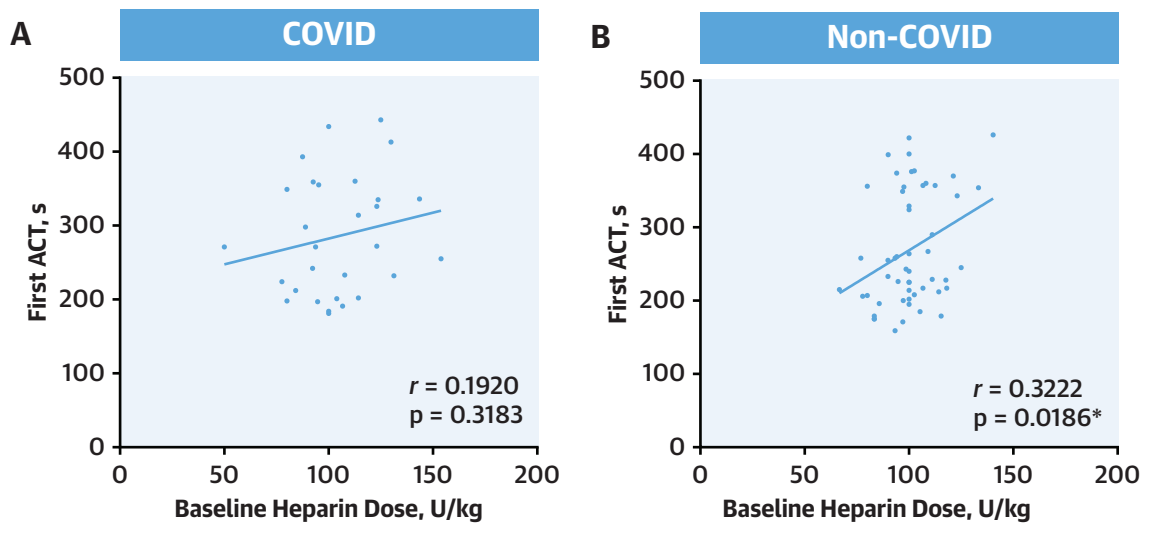
FIGURE 1 Correlation Between Baseline Weight-Adjusted Heparin Dose and ACT



Correlation between baseline weight-adjusted heparin dose (U/kg) and first activated clotting time (ACT) (s) measured after a 10- to 15-min interval in the **(A)** COVID-19 ST-segment elevation myocardial infarction (STEMI) group ($p = 0.3183$) and **(B)** non–COVID-19 STEMI group ($p = 0.0186$). *$p < 0.05$.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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