

#ISICEM23: Effects of Therapeutic-Dose Heparin in Hospitalised Patients With COVID-19



At the #ISICEM23 this week in Brussels, the benefits and harms of therapeutic-dose heparin varied by hospitalised COVID-19 patient characteristics were discussed, and the importance of considering the heterogeneity of treatment effect (HTE) in the design and analysis of randomised clinical trials was highlighted.

To date, RCTs that have tested therapeutic-dose heparin in COVID-19 patients have produced inconsistent results. This could be because of the HTE. A better understanding of this effect could help doctors make personalised treatment decisions for COVID-19 patients.

This study aimed to assess the HTE of therapeutic-dose heparin and compare different methods for evaluating this effect. This was an exploratory analysis of a large clinical trial that involved 3,320 COVID-19 patients hospitalised and treated with therapeutic-dose heparin or usual care pharmacologic thromboprophylaxis. The trial was conducted across multiple regions between April 2020 and January 2021.

The study evaluated the HTE of heparin treatment using three methods: conventional subgroup analyses of baseline characteristics, a multivariable outcome prediction model (risk-based approach), and a multivariable causal forest model (effect-based approach). Study participants were randomly assigned to receive either therapeutic-dose heparin or usual care pharmacologic thromboprophylaxis.

The study used two primary outcome measures: (1) organ support-free days, which were calculated by assigning a value of -1 to patients who died during hospitalisation and counting the number of days free from cardiovascular or respiratory organ support up to day 21 for patients who survived until hospital discharge, and (2) hospital survival.

As per the findings, therapeutic-dose heparin treatment was not associated with an increase in organ support-free days in the overall population. However, conventional subgroup analyses revealed that the treatment effect varied among patients requiring organ support at baseline, between females and males, and between patients with lower and higher BMI. The risk-based analysis showed that patients at the lowest risk of poor outcome had the highest propensity for benefit from heparin, while those at the highest risk were most likely to be harmed. The effect-based analysis identified a subset of patients at high risk of harm, who tended to have a high BMI and were more likely to require organ support at baseline.

Overall, these findings show that the effect of therapeutic-dose heparin among patients hospitalised for COVID-19 was heterogeneous. The three approaches used to assess HTE showed that heparin was more likely to be beneficial in patients who were less severely ill at presentation or had lower BMI and more likely to be harmful in sicker patients and those with higher BMI. These findings highlight the importance of considering HTE in the design and analysis of randomised clinical trials.

Source: [JAMA](#)

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