Optimal thromboprophylaxis and anticoagulant strategies in patients with COVID-19 pneumonia. The PROTHROMCOVID Trial

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Introduction: Hospitalized patients with COVID-19 are at increased risk of venous and arterial thrombosis, ARDS, and death. The optimal dosage of thromboprophylaxis in patients is unknown.

Objective: To evaluate the efficacy and safety of tinzaparin in prophylactic, intermediate and therapeutic doses in non-critical patients admitted for COVID-19 pneumonia.

Design, Setting, and Participants: The PROTHROMCOVID multicenter randomized clinical trial enrolled noncritical hospitalized adult patients with COVID-19 pneumonia from February 1, 2021, to September 30, 2021, at 18 centers in Spain.

Methods: Patients were randomized to prophylactic tinzaparin 4500IU or intermediate dose 100IU/kg or therapeutic tinzaparin 175IU/kg during hospitalization, followed by 7 days of prophylactic tinzaparin at discharge. The patients were stratified at the time of randomization according to age, sex and the presence or absence of hypertension.The primary efficacy outcome was a composite endpoint of symptomatic systemic thrombotic events, need for invasive or non invasive mechanical ventilation or not, including high-flow nasal cannula oxygen, or death within 30 days. The main safety outcome was major bleeding at 30 days. Data were collected and adjudicated locally by non-blinded investigators through imaging, laboratory, and health record data.

Results: Of 311 patients randomized, 300 were included in the analysis (mean [SD]age, 56.7 [14.6] years; men, 182 [60.7%]; women, 118 [39.3%]). 106 patients (35.33%) were assigned to the prophylaxis group, 91 patients (30.33%) were allocated to the intermediate dose group and 103 patients (34.33%) were randomized to the anticoagulant dose group. The composite endpoint thrombotic event, need for invasive (IMV) or non-invasive mechanical ventilation (NIV) or HFT via nasal cannula or death at 30 days from randomization occurred in 58 patients (19.3%) of the whole population, 19 patients (17.09%) in prophylactic group, 20 (21.98%) in intermediate group and 19 (18.45%) in therapeutic group (P=0.72). No major bleeding were reported in the trial and non-major bleeding occurred in 5 patients (4.71%) in prophilactic, in 3 patients (3.2%) in intermediate arm and in 3 patients (2.9%) in therapeutic, without significant differences in each group (P=0.31).

Conclusions: In non-critically ill patients with COVID 19, intermediate or full-dose of tinzaparin do not appear to offer benefit over standard prophylactic doses IU in the likelihood of thrombotic event, non-invasive ventilation or high-flow oxygen, or death.