

Role of heparin prophylaxis at different doses in patients with COVID-19 and respiratory failure: a systematic review and meta-analysis

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Background: Venous thromboembolism (VTE) is common in patients with coronavirus disease-2019 (COVID-19). The use of heparin at higher doses than prophylactic is advocated, but the optimal regimens remain unknown due to the balance between prevention of thromboembolic events and bleeding risks.

Objective: To systematically review and perform a meta-analysis aimed at evaluating the risk of VTE and of major bleeding (MB) in patients with respiratory failure due to COVID-19 according to heparin doses.

Methods: We performed a systematic search in MEDLINE up until 22 March 2021. Studies on patients with respiratory failure due to COVID-19 were included if reported on study outcomes according to standard prophylactic and to higher heparin doses and included more than 10 patients. Study primary outcome was VTE; secondary outcomes were MB, all-cause death, fatal bleeding and fatal pulmonary embolism (PE).

Results: Overall, 2 randomized and 16 observational studies were selected (3458 patients). In 13 studies (2492 patients) VTE events were similar in patients receiving standard prophylaxis or higher heparin doses (RR

1.06, 95% CI 0.58–1.95, I² 87%; only randomized studies RR 1.72, 95% CI 0.78–3.81, I² 54%). 16 studies (3174) reporting on MB and showed a significant reduction in favor of standard heparin prophylaxis (RR 0.39, 95% CI 0.28–0.53, I² 8%). No differences were observed for overall mortality according to heparin doses (RR 1.11, 95% CI 0.88–1.40, I² 68%; in 8 studies, 2448 patients). Similarly, no differences were observed for fatal bleedings and fatal PEs.

In the subanalysis of studies reporting only on intensive care unit patients (ICU) an increase in the risk of VTE (RR 1.86, 95% CI 1.28–2.72, I² 18%) and a reduction on the risk of MB (RR 0.60, 95% CI 0.40–0.90, I² 0%) were observed in patients receiving standard heparin doses compared to higher doses. Overall mortality was similar (RR 1.09, 95% CI 0.86–1.39, I² 64%).

Conclusion: Different doses of heparin prophylaxis seem to not affect the risk of VTE in the overall patients with COVID-19 and respiratory failure. In studies reporting only on ICU patients the risk of VTE was lower when higher heparin doses were used compared to standard doses, but with no advantage in overall death and with an increase of MBs.