

UAMS Journal Club Summary

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Incidence Rate of VTE in COVID-19 Patients

Clinical Bottom Line

The true risk of thromboembolism in the setting of infection with COVID-19 is unclear due to flaws in the published studies. Both meta-analyses included here have a high degree of heterogeneity. We concluded that we are unsure if there is a higher risk of VTE with COVID and that higher quality studies are needed in this area.

PICO Question Is COVID-19 associated with an increased risk of thromboembolism in hospitalized patients?

P- Patients hospitalized with COVID-19

I – No intervention

C- No comparison

O- Patients who develop thromboembolism

Background

Study 1

Jiménez D, García-Sánchez A, Rali P, Muriel A, Bikdeli B, Ruiz-Artacho P, Le Mao R, Rodríguez C, Hunt BJ, Monreal M. Incidence of VTE and Bleeding Among Hospitalized Patients With Coronavirus Disease 2019: A Systematic Review and Meta-analysis. *Chest*. 2021 Mar;159(3):1182-1196. doi: 10.1016/j.chest.2020.11.005. Epub 2020 Nov 17. PMID: 33217420; PMCID: PMC7670889.

Pubmed link:

<https://pubmed.ncbi.nlm.nih.gov/33217420/>

The Basics:

This was a Systemic Review and Meta-Analysis evaluating the rates of VTE and bleeding in hospitalized patients with COVID-19. Reports of high incidence rates of VTE in several individual studies have gained traction in medical circles and have led to many physicians initiating therapeutic anticoagulation in COVID patients. However, the true rate of VTE is unknown in these patients, so the authors sought to analyze the current studies on the topic to provide a more accurate rate of VTE in this meta-analysis. They did not compare these rates to hospitalized patients without COVID.

Methods:

15 standard sources and COVID-19-specific sources were searched between January 1, 2020, and July 31, 2020. Incidence estimates were pooled by using random effects meta-analyses. Heterogeneity was evaluated by using the I^2 statistic, and publication bias was assessed by using the Begg and Egger tests.

Results:

49 studies were ultimately included in this meta-analysis which included 18,093 total patients. Estimates for VTE incidence ranged from 0% to 85.4%, and the random effects overall pooled-estimated incidence of VTE was 17.0% (95% CI, 13.4 to 20.9), with high heterogeneity ($I^2 = 97\%$; $P < .001$). They also evaluated bleeding risk which showed a range between 2.7% to 21.6%, and the random effects overall pooled-estimated incidence of bleeding was 7.8% (95% CI, 2.6 to 15.3), with high heterogeneity ($I^2 = 95\%$; $P < .001$). They also used subgroup analyses on the incidence of VTE which showed a higher rate in ICU patients (27.9%) compared to patients on the wards (7.1%).

Limitations/Bias:

One limitation is that this study did not include mortality data for these patients, so it is unknown if there is any correlation between VTE events and mortality. Another limitation is the high heterogeneity among studies which calls into question whether these studies should have been grouped together within this meta-analysis. The study's authors also state that "lack of independent adjudication might have introduced significant biases into this meta-analysis". This analysis also contained mostly retrospective studies which can inherently introduce bias.

Study 2

Malas MB, Naazie IN, Elsayed N, Mathlouthi A, Marmor R, Clary B. Thromboembolism risk of COVID-19 is high and associated with a higher risk of mortality: A systematic review and meta-analysis. *EClinicalMedicine*. 2020 Dec;29:100639. doi: 10.1016/j.eclinm.2020.100639. Epub 2020 Nov 20. PMID: 33251499; PMCID: PMC7679115.

Pubmed link: <https://pubmed.ncbi.nlm.nih.gov/33251499/>

The Basics: This was a systematic review and meta analysis performed with the objective of estimating overall rates of thromboembolism in COVID-19 and determine the association of thromboembolism with mortality among patients with covid. Primary outcomes included rates of both venous and arterial thromboembolism. This was the first systematic review and meta-analysis to provide pooled estimates of both the venous and arterial thromboembolism rates.

Methods: A search of Pubmed, Cochrane, and Embase was performed and concluded on June 12, 2020. Screening of initial studies was performed by 2 independent investigators. Studies screened for full text were included if the rate of a thromboembolic event could be calculated based on the number of vascular events and the number of patients in the overall cohort. Disagreements between the two investigators were resolved by consensus and/or discussion

with a third investigator. All studies were evaluated with tools to assess the methodologic quality.

Results: Of 425 citations obtained from literature search, 50 full-text studies were screened. Eight were excluded, leaving 42 studies included in the analysis. Overall VTE rate was 21% (95% CI:17-26%) in all patients and 5% (95% CI:3-8%) in non-ICU patients. Rate of DVT was reported by 28 studies with an overall rate of 20% (95% CI: 16-23%). Overall rate of PE was 13% (95% CI: 11-16%). Overall rate of ATE was 2% (95% CI 2-4%). Mortality rate was 23% (95% CI: 14-23%) in those with thromboembolism and 13% (95% CI: 6-22%) in those without thromboembolism. Pooled odds of mortality were 74% higher in patients who developed TE compared to those who did not (OR 1.74; 95% CI: 1.01-2.98; P = 0.04).

Limitations/Bias: While this analysis did show increased risk of thromboembolism, the quality of the data is questionable. Studies included had very high rates of heterogeneity, higher than would normally be acceptable, as evidenced by the lowest I^2 value of 77% and most I^2 values being over 90%. Results were also not precise which is reflected in the wide confidence intervals. Most of the data was retrospective and investigators assumed correlation without controlling for confounders. Previous studies have estimated venous thromboembolism risk as high as 15.5% in hospitalized patients, and this study did not compare covid patients to non-covid patients.