

Received: 18 January 2021 | Accepted: 18 January 2021

DOI: 10.1002/ajh.26102

**RESEARCH ARTICLE**



# Intermediate-dose anticoagulation, aspirin, and in-hospital mortality in COVID-19: A propensity score-matched analysis

Matthew L. Meizlish<sup>1</sup>  | George Goshua<sup>2</sup>  | Yiwen Liu<sup>3</sup> | Rebecca Fine<sup>4</sup> |  
Kejal Amin<sup>5</sup> | Eric Chang<sup>2</sup> | Nicholas DeFilippo<sup>5,6</sup> | Craig Keating<sup>7</sup> | Yuxin Liu<sup>2</sup> |  
Michael Mankbadi<sup>4</sup> | Dayna McManus<sup>5</sup> | Stephen Y. Wang<sup>4</sup> | Christina Price<sup>8</sup> |  
Robert D. Bona<sup>2</sup> | Cassius Iyad Ochoa Chara<sup>9</sup> | Hyung J. Chun<sup>10</sup> |  
Alexander B. Pine<sup>2</sup> | Henry M. Rinder<sup>2,11</sup> | Jonathan M. Siner<sup>12</sup> |  
Donna S. Neuberg<sup>3</sup> | Kent A. Owusu<sup>5,13</sup> | Alfred Ian Lee<sup>2</sup> 

# Background

- Thrombosis is among the most devastating complications of COVID19.
- A common global practice has been to administer escalated intensities of antithrombotic therapy beyond standard prophylactic-dose anticoagulation in hospitalized COVID-19 patients.
- To date, no large-scale study has compared the effects of intermediate- versus prophylactic-dose anticoagulation.
- Regarding antiplatelet therapy, no consensus guidelines are available regarding aspirin use in COVID-19, reflecting a paucity of data in this regard.

# AIM of the study

- To examine the impact of intermediate-dose anticoagulation and aspirin on in-hospital mortality in COVID-19 patients.

# Methods

- Retrospective study
- Two separate, cohorts of patients:
  - who received intermediate- or prophylactic-dose anticoagulation (“anticoagulation cohort”, N = 1624);
  - who were not on home antiplatelet therapy and received either in-hospital aspirin or no antiplatelet therapy (“aspirin cohort”, N = 1956).
- The primary outcome was cumulative incidence of in-hospital death.

# Results (I)

- The overall study cohort consisted of 2785 patients .
- Half of patients were male (50.1%; N = 1396).
- The majority were over 60 years old (58.4%; N = 1627).
- Among all patients, 13.8% (N = 383) died in the hospital; 83.7% (N = 2330) were discharged alive, while 2.6% (N = 72) remained in the hospital at the time of data abstraction.
- Age > 60, male sex, obesity, and the maximum D-dimer level during hospitalization (DDmax) were significantly associated with in-hospital death, in keeping with prior studies.

**TABLE 1** Multivariable analysis of in-hospital death in the overall study cohort

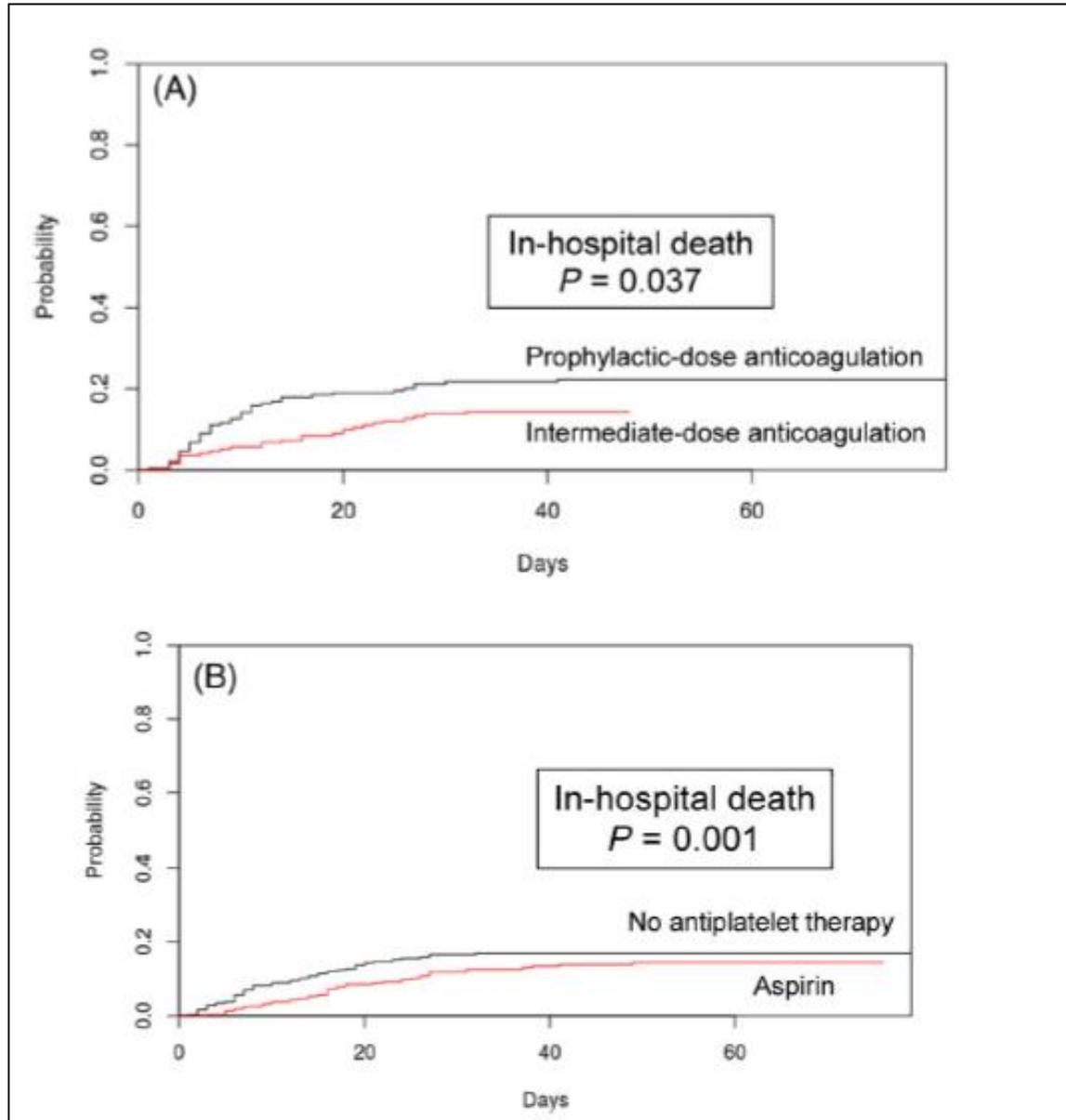
		Cumulative incidence of in-hospital death (competing risks model)		
		HR for death	CI	p value
Age > 60 years		3.545	2.599–4.836	< .001
Male sex		1.315	1.070–1.618	.009
Obesity		1.356	1.101–1.670	.004
Cardiovascular disease		1.014	0.799–1.286	.91
African-American		0.850	0.670–1.077	.18
DDmax		1.040	1.030–1.051	< .001
RI on admission	Quartile 1	6.713	4.860–9.274	< .001
	Quartile 2	2.764	1.958–3.903	< .001

Note: Multivariable regression analysis was performed within the overall study cohort to examine the association of in-hospital death with covariates. Cumulative incidence of in-hospital death was evaluated in a competing risks model with hospital discharge, and hazard ratios (HR) for in-hospital death were reported. For the maximum D-dimer level during hospitalization (DDmax), the hazard ratio represents the effect of an increase of one fibrinogen equivalent unit.

Abbreviations: CI, 95% confidence interval; DDmax, maximum D-dimer level during hospitalization; HR, hazard ratio; RI, Rothman Index.

## Results (II)

- Treatment with intermediate- compared to prophylactic-dose anticoagulation was associated with a significantly lower cumulative incidence of in-hospital death on multivariable regression (HR 0.518 [0.308–0.872] ).
- The use of in-hospital aspirin compared to no antiplatelet therapy was associated with a significantly lower cumulative incidence of in-hospital death on multivariable regression (HR 0.036 [0.002–0.576]).



**FIGURE 1** Cumulative incidence of in-hospital death among propensity score-matched patients (A) in the anticoagulation cohort, comparing intermediate- versus prophylactic-dose anticoagulation, and (B) in the aspirin cohort admitted after May 18, 2020, comparing in-hospital aspirin versus no antiplatelet therapy. (A) Patients in the anticoagulation cohort were propensity score matched for age, maximum D-dimer level, admission Rothman Index score, body mass index, and African-American race using a random number seed and a caliper width of 0.25. (B) Patients in the aspirin cohort admitted after May 18 were propensity score matched for age, maximum D-dimer level, and admission Rothman Index score. In each panel,  $p$  values from Gray's test describe differences in cumulative incidence functions between treatment groups [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

# Conclusions

- In this large, observational study of hospitalized patients with COVID-19, using propensity score matching and multivariable regression analyses, a mortality benefit with intermediate- compared to prophylactic-dose anticoagulation and, separately, with in-hospital aspirin compared to no antiplatelet therapy was observed.
- These findings suggest that increased-intensity anticoagulation and antiplatelet therapy may be beneficial in the treatment of COVID-19.
- Additional studies are warranted to definitively elucidate the impact of these therapies in COVID-19.