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Sex Differences in Thrombosis and Mortality in Patients Hospitalized for COVID-19

Tanya Wilcox, MD, Nathaniel R. Smilowitz, MD, MS, Bilaloglu Seda, MS, Yuhe Xia, MS, Judith Hochman, MD, and Jeffrey S. Berger, MD, MS*

Gender-specific differences in thrombosis have been reported in hospitalized patients with COVID-19. We sought to investigate the influence of age on the relation between gender and incident thrombosis or death in COVID-19. We identified consecutive adults aged ≥18 years hospitalized with COVID-19 from March 1, 2020, to April 17, 2020, at a large New York health system. In-hospital thrombosis and all-cause mortality were evaluated by gender and stratified by age group. Logistic regression models were generated to estimate the odds of thrombosis or death after multivariable adjustment. In 3,334 patients hospitalized with COVID-19, 61% were men. Death or thrombosis occurred in 34% of hospitalizations and was more common in men (36% vs 29% in women, p < 0.001; adjusted odds ratio [aOR] 1.61, 95% confidence interval [CI] 1.36 to 1.91). When stratified by age, men had a higher incidence of death or thrombosis in younger patients (aged 18 to 54 years: 21% vs 9%, aOR 3.17, 95% CI 2.06 to 5.01; aged 55 to 74 years: 39% vs 28%, aOR 1.63, 95% CI 1.28 to 2.10), but not older patients (aged ≥75 years: 55% vs 48%; aOR 1.20, 95% CI 0.90 to 1.59) (interaction p value: 0.01). For the individual end points, men were at higher risk of thrombosis (19% vs 12%; aOR 1.65, 95% CI 1.33 to 2.05) and mortality (26% vs 23%; aOR 1.41, 95% CI 1.17 to 1.69) than women, and gender-specific differences were attenuated with older age. Associations between thrombosis and mortality were most striking in younger patients (aged 18 to 54 years, aOR 8.25; aged 55 to 74 years, aOR 2.38; aged >75 years, aOR 1.88; p for interaction <0.001) but did not differ by gender. In conclusion, the risk of thrombosis or death in COVID-19 is higher in men compared with women and is most apparent in younger age groups. © 2022 Published by Elsevier Inc. (Am J Cardiol 2022;170:112–117)

Patients hospitalized with COVID-19 are at risk for thrombotic complications, including deep vein thrombosis (DVT), pulmonary embolism (PE), ischemic stroke, and myocardial infarction (MI). Thrombosis occurs in 16% to 31% of patients hospitalized with COVID-19 and is associated with critical illness and all-cause mortality. Older age and male gender are established risk factors for severity of illness and mortality associated with COVID-19. However, the influence of age on gender-specific differences in COVID-19 is unknown. Age-dependent gender-specific differences in outcomes have been reported in cardiovascular diseases before the COVID-19 pandemic. In patients with acute MI, for example, younger but not older women have excess in-hospital mortality compared with men of the same age. In community cohorts, women of reproductive age have higher risks of venous thrombosis and lower risks of arterial thrombosis compared with age-matched men. This study aimed to investigate the influence of age on the relation between gender and incident thrombosis or death in patients hospitalized with COVID-19, after accounting for differences in demographics, clinical comorbidities, and disease presentation.

Methods

The study was approved by the New York University (NYU) Grossman School of Medicine institutional review board. Consecutive adults aged ≥18 years with COVID-19 admitted to NYU Langone Health, a large health care system in New York, between March 1, 2020, and April 17, 2020, were identified. All patients were required to have a positive nucleic acid amplification test for SARS-CoV-2 during hospitalization and a diagnosis of COVID-19. Patient demographics and clinical comorbidities were determined through a systematic query of the electronic health record, as previously described.

Thrombotic events of interest included those occurring in both the venous and arterial circulation. Venous thromboembolism (VTE) was defined as DVT or PE, and arterial thrombosis was defined as ischemic stroke, myocardial infarction, or other systemic thromboembolism. Events were identified using an open-source natural language processing tool to search clinical documentation and radiology reports. Additional thrombotic events were identified through a query of the relevant International Classification Of Diseases, 10th Revision codes, and review of echocardiography reports. All suspected thromboses were confirmed.

The Leon H. Charney Division of Cardiology, Department of Medicine, New York University School of Medicine, New York, New York.

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*Corresponding author: Tel: XXX; fax: XXX.

E-mail address: jeffrey.berger@nyumc.org (J.S. Berger).
by a manual review of the medical record. In-hospital mortality or discharge to hospice was determined for all patients. Owing to the potential for multiple contributing causes in critically ill patients with multi-organ dysfunction, adjudication of the cause of death was not performed. Fatal thrombosis was defined as any arterial or venous thrombosis that occurred in a patient who subsequently died in hospital. Given the competing risk of death, we evaluated the composite end point of death or thrombosis in our primary analyses. Critical illness was defined as mechanical ventilation or transfer to the intensive care unit during hospitalization for COVID-19.

Categorical data are shown as frequencies and proportions and compared by chi-square tests. Continuous data are expressed as median (interquartile range) and compared by Mood’s test. The incidence of thrombosis and in-hospital mortality was evaluated in subgroups by age and gender. Multivariable logistic regression models were generated to estimate the odds of thrombosis, death, or both by age subgroup and gender, adjusted for race/ethnicity, body mass index (BMI), smoking, clinical comorbidities including hypertension, dyslipidemia, diabetes mellitus, coronary artery disease, a history of MI, heart failure, atrial fibrillation, peripheral artery disease, known cerebrovascular disease, chronic obstructive pulmonary disease, kidney disease, any history of malignancy, and initial d-dimer concentration at the time of hospital presentation. Multivariable logistic regression models were also generated to assess risk factors associated with thrombosis in gender-stratified cohorts, adjusted for demographics and covariates as previously described. The influence of age on the relation between gender and incident thrombosis or death was evaluated by adding an interaction term for age subgroup (18 to 54, 55 to 74, and ≥75 years) and gender to the multivariable logistic regression models. Statistical analyses were conducted using R Studio Software Version 3.5.1 (The R Foundation for Statistical Computing, Vienna, Austria). Two-tailed p values <0.05 were considered statistically significant.

Results

In 3,334 patients admitted with COVID-19, 2,014 (61%) were men. Patient characteristics by age and gender are listed in Table 1. A greater proportion of women were of Black race compared with men. Across all age groups, men had a higher prevalence of coronary artery disease than women. In patients ≥55 years of age, smoking was more common in men. Women had lower median BMIs compared with men in patients aged <55 years (Table 1).

The composite end point of death or thrombosis occurred in 34% patients hospitalized with COVID-19 and was more common in men than women (36% vs 29%, p <0.001). After adjusting for age, race/ethnicity, BMI, smoking,
clinical comorbidities, and initial D-dimer concentration, men were 65% more likely to develop death or thrombosis than women (adjusted odds ratio [aOR] 1.65, 95% confidence interval [CI] 1.32 to 2.05). When stratified by age, men had a greater risk of death or thrombosis than women in patients aged 18 to 54 years (21% vs 9%, p <0.001; aOR 3.17, 95% CI 2.06 to 5.01) and 55 to 74 years (39% vs 28%, p <0.001 aOR 1.63, 95% CI 1.28 to 2.10), but not older adults aged ≥75 years (55% vs 48% p = 0.07; aOR 1.20, 95% CI 0.90 to 1.59; p for interaction = 0.01; Figures 1 and 2).

A greater proportion of men hospitalized with COVID-19 had an in-hospital thrombotic event compared with women (19% vs 12%, p <0.001; aOR 1.65, 95% CI 1.33 to 2.05). A consistent gender-specific increased risk in men was observed for both venous (8% vs 4%, p <0.001; aOR 1.84, 95% CI 1.30 to 2.65) and arterial (12% vs 9%, p=0.006; aOR 1.45, 95% CI 1.13 to 1.87) thrombosis. When evaluated by subtype of thrombosis, the incidence of MI, DVT, and PE was higher in men compared with women (Supplementary Figure 1). When analyzed by age, men had a greater risk of any thrombosis than women in younger cohorts (aged 18 to 54 years: 15% vs 6%, aOR 3.85, 95% CI 2.35 to 6.94; aged 55 to 74 years: 20% vs 12%, aOR 1.65, 95% CI 1.18 to 2.33), but not older cohorts (aged ≥75 years: 21% vs 18% p =0.37; aOR 1.08, 95% CI 0.75 to 1.56; p for interaction = 0.01) (Figures 1 and 2). Similar findings were observed for VTE and arterial thrombotic events, with younger, but not older men having significantly higher risk of VTE (aged 18 to 54 years: 8% vs 3%, aOR 2.66, 95% CI 1.51 to 4.93; aged 55 to 74 years: 10% vs 5%, aOR 1.43, 95% CI 1.10 to 1.89; aged >75 years: 3% vs 3%, aOR) and arterial thrombosis (aged 18 to 54 years: 9% vs 3%, aOR 3.78, 95% CI 1.79 to 8.78; aged 55 to 74 years: 17% vs 12%, aOR 1.46, 95% CI 0.98 to 2.23; aged >75 years: 13% vs 18%, aOR 1.11, 95% CI 0.76 to 1.64) than women (Supplementary Figures 2 and 3). Gender-specific risk factors for any thrombosis in patients with COVID-19 are listed in Supplementary Table 1. In women, but not men, older age was an independent risk factor for thrombosis. Coronary artery disease and elevated initial D-dimer concentrations were associated with increased odds for thrombosis in both men and women (Supplementary Table 1).

All-cause mortality was higher in men hospitalized with COVID-19 compared with women (26% vs 22%, p = 0.03, aOR 1.18, 95% CI 1.00 to 1.41). Gender differences in mortality were observed; however after multivariable adjustment, no significant age-gender interaction was observed (p for interaction = 0.30; Figures 1 and 2). In patients with COVID-19 with thrombosis, outcomes were poor. Patients with thrombosis versus without had a higher incidence of critical illness (49% vs 23%, p <0.001, aOR 3.21, 95% CI 2.63 to 3.92) and in-hospital mortality (43% vs 21%, p <0.001, aOR 2.66, 95% CI 2.18 to 3.26; Table 2). The association between thrombosis and mortality was comparable in men (43% vs 22% without thrombosis; aOR 2.54, 95% CI 2.00 to 3.25) and women (44% vs 20%
without thrombosis; aOR 3.02, 95% CI 2.08 to 4.37; p for interaction = 0.412; Table 2). The risk of mortality in patients with a thrombotic event was significant across all age groups (aged 18 to 55 years: 6% vs 2%, p <0.001, aOR 8.25, 95% CI 4.69 to 14.63; aged 54 to 75 years: 19% vs 9%, p <0.001, aOR 2.38, 95% CI 1.77 to 3.23; aged >75 years: 18% vs 10%, p <0.001, aOR 1.88, 95% CI 1.32 to 2.70); however, the association between thrombosis and death was most striking in younger patients (p for interaction p <0.001; Table 2).

Discussion

In this retrospective cohort of adults hospitalized with COVID-19, men had a higher risk of death or thrombosis than women, with gender differences most pronounced in the youngest patients and attenuated with older age. Gender differences were also observed in the individual end point of thrombosis, with a nearly 2-fold excess risk of VTE and a 3-fold risk of arterial events in men compared with women. To our knowledge, this is the first study to explore age and gender differences in the incidence of thrombotic events or death in COVID-19. Our data provide compelling evidence that thrombosis, a potentially fatal complication of SARS-CoV-2 infection, may contribute to the observed gender differences in mortality from COVID-19.

Observations reported in this analysis are consistent with previous studies demonstrating gender differences in COVID-19 outcomes.4 As of September 2021, men accounted for 57% of COVID-related deaths and 64% of intensive care unit admissions, according to dis-aggregated gender data available in 109 countries.11,18 Similar to our findings, recent propensity-matched survival analysis showed that comorbid conditions could not fully explain observed gender differences in mortality, however, interaction testing by age subgroups was not performed.9 To our knowledge, previous studies have not investigated the influence of age on the association between gender and clinical outcomes, including thrombosis.

We observed a significant age-gender interaction on the outcome of thrombosis or death during hospitalization for COVID-19. This observation cannot be explained by gender differences in traditional cardiovascular risk factors in our cohort, as younger women had a similar prevalence of cardiovascular risk factors compared with younger men. Differences in female sex hormones concentrations, including the systemic effects of estrogen, could account for

![Figure 2. Adjusted Odds of Events in Men Relative to Women Hospitalized with COVID-19 by Age Group.](image-url)
favorable outcomes observed in younger women compared with men, but this requires further study.

Inflammation and sepsis can significantly increase risks of venous and arterial thrombosis. Gender differences in inflammation in response to COVID-19 have been reported, but the impact of the inflammatory response on thrombotic outcomes in COVID-19 is unknown. In addition, modulation of the renin-angiotensin-aldosterone axis, endothelial responses to inflammation, and coagulation profiles also vary by gender and age, and may also contribute to differences in thrombotic risk.

Consistent with previous studies, COVID-19 thrombosis was significantly associated with in-hospital mortality in men and women, and this relation was most pronounced in younger patients of both genders. This may reflect competing risks of death from nonvascular causes in older patients with COVID-19. Alternatively, younger patients may be more likely to develop a large burden of thrombus associated with severe hemodynamic consequences in the setting of COVID-19.

This retrospective observational study has several important limitations. First, we were unable to account for unmeasured confounders associated with thrombosis, including recent surgery, trauma, thrombophilia, or immobility. Although all patients in this cohort were hospitalized with COVID-19, we cannot exclude unmeasured gender differences in disease severity and immobility, a known risk factor for VTE. Even so, arterial thromboses were also more common in men than women, suggesting that immobility alone does not explain the observed differences in thrombotic risk associated with COVID-19. Second, we were unable to assess the use of prophylactic versus therapeutic anticoagulation during hospitalization. Patients in the study were admitted before widespread recognition of thrombotic risk in COVID-19, anticoagulation strategies for COVID-19 were not standardized at the time of this study, and gender differences in antithrombotic prescribing cannot be excluded. Similarly, our study does not report gender differences in steroid administration, and large population-based case-control studies have demonstrated that glucocorticoid use is associated with VTE.

However, patients in this study were enrolled before the discovery of risk reductions associated with immunosuppressive therapy, and steroids were not routinely prescribed. Third, we were unable to account for missed diagnoses of thrombosis, which may have occurred without confirmatory diagnostic imaging. Thus, detection bias is a limitation of our study. Fourth, vascular causes of death were not adjudicated in the current analysis, and all-cause in-hospital mortality was reported instead. Finally, the incidence of out-of-hospital thrombosis could not be determined, and long-term mortality was not evaluated. Although practice patterns have changed significantly since the beginning of the pandemic, our study speaks to the natural history of untreated COVID-19 infection in unvaccinated patients.

In conclusion, men hospitalized with COVID-19 are at greater risk of thrombosis and death than women, and gender-specific differences are most pronounced in younger age groups. Outcomes of men and women with COVID-19-associated thrombosis are poor. Additional investigations of SARS-CoV-2 pathophysiology and host response are needed to inform the mechanisms of age and gender-
specific differences in cardiovascular outcomes and thrombotic risk in COVID-19.

Declaration of Competing Interest

The authors have no conflicts of interest to declare.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2022.01.024.

1. Bilaloglu S, Aphinianaphongs Y, Jones S, Iturrate E, Hochman J, Berger JS. Thrombosis in hospitalized patients with COVID-19 in a New York City health system. JAMA 2020;324(8):799–801.

2. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. J Thromb Haemost 2020;18(6):1421–1424.

3. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggan E, Nigoghossian CD, Ageno W, Madjidi M, Guo Y, Tang LV, Hu Y, Giri J, Cushman M, Quéré I, Dimakakos EP, Gibson CM, Lippi G, Favalo negro EJ, Fareed J, Caprini JA, Tafur AJ, Burton FR, Francesc DP, Wang EY, Falanga A, McIntrock C, Hunt BJ, Spyropoulos AC, Barnes BD, Eikelboom JW, Weinberg I, Schulman S, Carrier M, Piazza G, Beckman JA, Steng PG, Stone GW, Rosenkranz S, Goldhaber SZ, Parikh SA, Monreal M, Krumholz HM, Kontodimatas SV, Weitz JI, Lip GYH. Global COVID-19 Thrombosis Collaborative Group, Endorsed by the ISTH, NART, ESVFM, and the IUA. Supported by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function, COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up. JACC State-of-the-Art Review. J Am Coll Cardiol 2020;75(23):2950–2973.

4. Klok FA, Kruip MJHA, Van der Meer NJM, Arbous MS, Gomers DAMP, Kant KM, Kaptein FHI, van Paassen J, Stals MAM, Huisman MV, Endeman H. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020;191:145–147.

5. Sharma G, Volgman AS, Michos ED. Sex differences in mortality from COVID-19 pandemic: are men vulnerable and women protected? JACC Case Rep 2020;2(9):1407–1410.

6. Xie J, Tong Z, Guan X, Du B, Qiu H. Clinical characteristics of patients who died of coronavirus disease 2019 in China. JAMA Netw Open 2020;3(6):e204419.

7. Peckham H, de Gruijter NM, Raine C, Radziszewska A, Ciurtin C, Manson S, EJ, Fareed J, Caprini JA, Tafur AJ, Burton FR, Francesc DP, Wang EY, Falanga A, McIntrock C, Hunt BJ, Spyropoulos AC, Barnes BD, Eikelboom JW, Weinberg I, Schulman S, Carrier M, Piazza G, Beckman JA, Steng PG, Stone GW, Rosenkranz S, Goldhaber SZ, Parikh SA, Monreal M, Krumholz HM, Kontodimatas SV, Weitz JI, Lip GYH. Global COVID-19 Thrombosis Collaborative Group, Endorsed by the ISTH, NART, ESVFM, and the IUA. Supported by the ESC Working Group on Pulmonary Circulation and Right Ventricular Function, COVID-19 and thrombotic or thromboembolic disease: implications for prevention, antithrombotic therapy, and follow-up. JACC State-of-the-Art Review. J Am Coll Cardiol 2020;75(23):2950–2973.

8. Xie J, Tong Z, Guan X, Du B, Qiu H. Clinical characteristics of patients who died of coronavirus disease 2019 in China. JAMA Netw Open 2020;3(6):e204419.

9. Alkhouli M, Nanjundappa A, Annie F, Bates MC, Bhatt DL. Sex differences in case fatality rate of COVID-19: insights from a multinational registry. Mayo Clin Proc 2020;95(8):1613–1620.

10. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, Cereda D, Coluacello A, Fori G, Fumagalli R, Iotti G, Lippi G, Previtali E, Bucciarelli P, Passamonti SM, Martinelli I. Risk factors for venous and arterial thrombosis. [Blood transfusion = Trasfusione sangue]. Transfus Sci 2020;55(3):453–462.

11. Roach RE, Cangemi SC, LiJjer WM. Differential risks in men and women for first and recurrent venous thrombosis: the role of genes and environment. J Thromb Haemost 2014;12(10):1593–1600.

12. Swartz J, Koziatek C, Theobald J, Smith S, Iturrate E. Creation of a simple natural language processing tool to support an imaging utilization quality dashboard. Int J Med Inform 2017;101:93–99.

13. Previtali E, Bucciarelli P, Passamonti SM, Martinelli I. Risk factors for venous and arterial thrombosis. [Blood transfusion = Trasfusione sangue]. Transfus Sci 2020;55(3):453–462.

14. Palareti G, Legnani C, Antonucci E, Cosmi B, Poli D, Testa S, Tosetto A, Ageno W, Falanga A, Ferrari PM, Pengo V, Prandoni P. DULCIS (D-dimer and Ultrasoundography in Combination Italian Study) Investigators. D-dimer testing, with gender-specific cutoff levels, is of value to assess the individual risk of venous thromboembolic recurrence in non-elderly patients of both genders: a post hoc analysis of the ducis study DULCIS study. Intern Emerg Med 2020;15(3):453–462.

15. Roach RE, Cangemi SC, LiJjer WM. Differential risks in men and women for first and recurrent venous thrombosis: the role of genes and environment. J Thromb Haemost 2014;12(10):1593–1600.

16. Swartz J, Koziatek C, Theobald J, Smith S, Iturrate E. Creation of a simple natural language processing tool to support an imaging utilization quality dashboard. Int J Med Inform 2017;101:93–99.

17. Previtali E, Bucciarelli P, Passamonti SM, Martinelli I. Risk factors for venous and arterial thrombosis. [Blood transfusion = Trasfusione sangue]. Transfus Sci 2020;55(3):453–462.

18. Haitao T, Verma NT, Ayekoon K, Jham H, Dissanayake S, Lawlor P. Thrombosis in hospitalized patients with COVID-19. Am Heart J 2021;233:91–95.

19. Bunders MJ, Altfeld M. Implications of sex differences in immunity for SARS-CoV-2 pathogenesis and design of therapeutic interventions. Immunity 2020;53(3):487–495.

20. Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. J Immunol 2017;198(10):4046–4053.

21. Verheul H, Klinman DM. Sex hormone levels correlate with the activity of cytokine-secreting cells in vivo. Immuno logic 2000;100(3):384–390.

22. Takahashi T, Ellingson MK, Wong P, Israelow B, Lucas C, Klein J, Silva J, Mao T, Oh JE, Tokuyama M, Lu P, Venkataraman A, Park A, Liu F, Meir A, Sun J, Wang WY, Easawon-Massana A, Wylie AL, Vogels CBP, Earnest R, Lapidus S, Ott IM, Moore AJ, Hale IMPACT Research Team, Shaw A, Fournier JB, Odio CD, Farhadian S, Dela Cruz C, Grubau NG, Schulz WL, Ring AM, Ko AI, Omer SB, Iwasaki A. Sex differences in immune responses that underlie COVID-19 disease outcomes. Nature 2020;588(7837):315–320.

23. Rathod K, Kapil V, Velmurugan S, Khambata R, Siddique U, Khan S, Gee L, Bansal J, Pirrola K, Shaw C, D’Acutis F, Colas R, Marelbel-Benedetti D, Dalli J, Arnold M. Sex differences in the inflammatory response and inflammation-induced vascular dysfunction. Lancet 2017;389(9240):315–320.

24. Beristain-Covarrubias N, Perez-Toledo M, Thomas MR, Henderson IR, Watson SP, Cunningham AF. Understanding infection-induced thrombosis: lessons learned from animal models. Front Immunol 2019;10:2569.

25. Schmidt M, Horvath-Puho E, Thomsen RW, Smeeth L, Sorensten HT. Acute infections and venous thromboembolism. J Intern Med 2012;271(6):608–618.

26. Zhou H, Hu Y, Li X, Wang W, Wang M, Xiao J, Yi Q. Assessment of the risk of venous thromboembolism in medical inpatients using the pauto prediction score and caprini risk assessment model. J Atheroscler Thromb 2018;25(11):1091–1104.

27. Johannesdottir SA, Horvath-Puhon E, Drekkers OM, Cangemi SC, Jergensen JOL, Ehrenstein V, Vandebroucke JP, Pedersen L, Sorensten HT. Use of glucocorticoids and risk of venous thromboembolism: A nationwide population-based case-control study. JAMA Intern Med 2013;173(9):743–752.

28. Recovery Collaborative Group, Horby P, Lim WS, Emerson JM, Mathias M, Bell JL, Linsell L, Stalpi A, Brightling C, Usiowski a, Elmahi E, Prudon B, Green C, Felton T, Chadwick D, Rege K, Fegan C, Chappell LC, Faust SN, Jaki T, Jeffery K, Montgomery A, Rowan K, Juszczak E, Baillie JK, Haynes R, Landray MJ. Dexamethasone in patients with COVID-19. N Engl J Med 2021;384(8):693–704.