Elevated D-Dimer Levels Are Associated With Increased Risk of Mortality in Coronavirus Disease 2019: A Systematic Review and Meta-Analysis

Siddharth Shah, MD,* Kuldeep Shah, MD,† Siddharth B. Patel, MBBS, MPH,‡ Foram S. Patel, MPH,§ Mohammed Osman, MD‖ Poonam Velagapudi, MD,¶ Mohit K. Turagam, MD,‖‖ Dhanunjaya Lakkireddy, MD,** and Jalaj Garg, MD, FACC, FESC††

Abstract: The 2019 novel coronavirus, declared a pandemic, has infected 2.6 million people as of April 27, 2020, and has resulted in the death of 181,938 people. D-dimer is an important prognostic tool, often elevated in patients with severe coronavirus disease-19 (COVID-19) infection and in those who suffered death. In this systematic review, we aimed to investigate the prognostic role of d-dimer in COVID-19-infected patients. We searched PubMed, Medline, Embase, Ovid, and Cochrane for studies reporting admission d-dimer levels in COVID-19 patients and its effect on mortality. Eighteen studies (16 retrospective and 2 prospective) with a total of 3682 patients met the inclusion criteria. The pooled weighted mean difference (WMD) demonstrated significantly elevated d-dimer levels in patients who died versus those who survived (WMD, 6.13 mg/L; 95% confidence interval [CI] 4.16–8.11; P < 0.001). Similarly, the pooled mean d-dimer levels were significantly elevated in patients with severe COVID-19 infection (WMD, 0.54 mg/L; 95% CI 0.28–0.80; P < 0.001). The risk of mortality was fourfold higher in patients with positive d-dimer versus negative d-dimer (risk ratio, 4.11; 95% CI, 2.48–6.84; P < 0.001) and the risk of developing severe disease was twofold higher in patients with positive d-dimer levels versus negative d-dimer (risk ratio, 2.04; 95% CI, 1.34–3.11; P < 0.001). Our meta-analysis demonstrates that patients with COVID-19 infection presenting with elevated d-dimer levels have an increased risk of severe disease and mortality.

Key Words: 2019-nCoV, D-dimer, severe COVID-19, mortality

Methods

Search Strategy

The reporting of this systematic review and meta-analysis complies with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines (Supplement Table 1, http://links.lww.com/CIR/A21).7

The initial search strategy was developed by 2 authors (S.S. and S.P.). We performed a systematic search, without language restriction, using PubMed, EMBASE, SCOPUS, Google Scholar, and 2 preprint servers (https://www.medrxiv.org and https://www.ssrn.com/index.cfm/en/coronavirus) from inception to April 16, 2020, for studies that reported d-dimer levels in COVID-19 patients. We utilized the “related articles” function in PubMed to find relevant articles that were missed by the initial search. Also, reference lists of the included studies were hand-searched to further locate relevant articles that were missed in the primary search. We used the following keywords and medical subject heading: “COVID-19,” “SARS-CoV-2,” “Wuhan coronavirus,” “Coronavirus 2019,” “2019 n-CoV,” “d-dimer,” “laboratory.”

Study Selection and Data Extraction

To be included in our systematic review and meta-analysis, the study had to fulfill the following criteria: (1) reported d-dimer levels in COVID-19 patients according to severity or including mortality as a clinical outcome; (2) included human subjects; and (3) studies in the English language. Single-arm studies, case reports, editorials, or systematic reviews were excluded. Two investigators (S.S. and S.P.)
independently performed the literature search and screened all titles and full-text versions of all relevant studies that met study inclusion criteria. The data from included studies were extracted using a standardized protocol and a data extraction form. Any discrepancies between the 2 investigators were resolved through consultation with the senior investigator (J.G.). Two independent reviewers (S.S. and S.P.) extracted the following data from the eligible studies: author name, study design, publication year, follow-up duration, number of patients, age, gender, diabetes mellitus (DM), hypertension, coronary artery disease (CAD), acute cardiac injury, arrhythmias, shock, and outcomes. The Newcastle Ottawa Risk bias assessment tool was used to appraise the quality of the included studies (Supplement Table 2, http://links.lww.com/CIR/A21).

OUTCOMES
Clinical Outcomes
The primary outcome of interest in our study was all-cause mortality and severity of COVID-19.

STATISTICAL ANALYSIS
For binary data, the Mantel-Haenszel (MH) risk ratio (RR) random-effects model (DerSimonian and Laird method) was used to summarize data between the 2 groups.6 For continuous data (e.g., d-dimer), studies that reported as the median and interquartile range, we first used the Wan method to estimate the mean and standard deviations.9 We then calculated the pooled weighted difference in means (WMD) using a random-effects model to evaluate the association of levels of d-dimer between the 2 groups. Higgins I-squared ($I^2$) statistic was used to assess the test of heterogeneity. A value of $I^2$ of 0%– 25% represented insignificant heterogeneity, 26%–50% represented low heterogeneity, 51%–75% represented moderate heterogeneity, and more than 75% represented high heterogeneity.10 A prespecified random-effects metaregression analysis was conducted for the primary outcome in relation to the baseline demographics, comorbid conditions, biomarkers to test the relationship between d-dimer and disease severity, and all-cause mortality. Publication bias was formally assessed using funnel plots and Egger’s linear regression test of funnel plot asymmetry. A 2-tailed $P \leq 0.05$ was considered statistically significant. Statistical analysis was performed using Comprehensive Meta-Analysis version 3.0 (Biostat Solutions, Inc. [BSSI], Frederick, MD).

RESULTS
Search Results
A total of 920 citations were identified during the initial search (Fig. 1). Nine hundred and two records were excluded. After a detailed evaluation of these studies, 12 studies met the inclusion criteria. We also included 6 manuscripts from 2 preprint servers (https://www.medrxiv.org and https://www.ssrn.com/index.cfm/en/coronavirus), to accommodate the rapidly evolving nature of information for COVID. We acknowledge that the manuscripts from these 2 sources are not peer reviewed. Eighteen articles of 3682 patients were included in the final analysis.

Study Characteristics
This systematic review and meta-analysis of 18 studies incorporated a total of 3682 patients. Six articles compared d-dimer levels upon admission in patients who survived versus those who died,11–16 1 article compared patients with elevated d-dimer level with those with normal d-dimer levels,17 and 11 articles compared severe versus nonsevere COVID-19 patients.18–28 All studies were retrospective15–27 except 2, which were prospective,11,28 and all were conducted in China in the year 2020.

Positive d-dimer was defined as a value above the normal reference range. Five studies11,12,14,19,26 considered levels $\geq 0.5$ mg/L as abnormal, 5 studies11,17,18,23,27 used $> 0.5$ mg/L as an abnormal value, 3 studies15,20,28 considered levels $> 0.55$ mg/L as abnormal, 2 studies11,24 considered levels $> 0.243$ mg/L as abnormal, and 3 studies16,22,25 gave only mean values of d-dimer (which were then used to calculate pooled WMD). The assay used to measure d-dimer was mentioned in only 1 study.27 Wherever necessary, the unit for d-dimer was converted to mg/L. Severe COVID-19 disease was defined in a patient with a respiratory rate $\geq 30$ beats/min (resting state) or a mean oxygen saturation of $\leq 93\%$ on room air or an arterial blood oxygen partial pressure ($PaO_2$)/oxygen concentration ($FiO_2$) $\leq 300$ mm Hg and was consistent across all studies. The severe group included patients with severe COVID-19 and/or those needing ICU care for acute respiratory failure requiring mechanical ventilation, or for shock, or multiorgan failure. Survived patients were defined as those who were discharged from the hospital following recovery, were still in-hospital at the end of follow-up period (6 studies),11–13,15–17 or those patients who survived at least 28 days from admission (1 study).14

Table 1 summarizes the baseline characteristics of 6 studies,11–13 which compared dead versus survived patients, and 1 study which compared patients with elevated d-dimer versus normal d-dimer levels. Among the 6 studies which compared dead versus survived patients, the mean age of the study population in this group was 62.5±14.8 years, and 56.3% were males. Overall, hypertension was the most common comorbidity (36.6%), followed by DM (16.8%) and CAD (11.7%). Shock was observed in 8.9% of patients.

Table 2 summarizes the baseline characteristics of 11 studies18–28 that compared severe versus nonsevere COVID-19 patients. The mean age of the study population was 49.9±17.2 years, and 54.6% were males. Overall, hypertension was the most common comorbidity (18.8%), followed by DM (9.2%) and CAD (3.9%). Shock was observed in 3.6% of patients, of which 2% of patients had septic shock. Shock was undefined in the other patients.

All-Cause Mortality
The data for d-dimer levels were available in 5 studies.11,13–16 The pooled mean d-dimer levels were significantly elevated in patients who died versus those who survived (WMD, 6.13 mg/L; 95% CI, 4.16–8.11; $P \leq 0.001$; $I^2 = 81.41\%$) (Fig. 2). No publication bias was observed (Egger’s $P = 0.39$, Supplement Figure 1, http://links.lww.com/CIR/A20). A meta-regression analysis demonstrated no significant associations between age, male sex, hypertension, DM, CAD, C-reactive protein, and troponin in COVID-19-infected patients who died versus those who survived (Table 3).

The risk of mortality was fourfold in patients with positive d-dimer versus negative d-dimer (21% vs 4.9%; RR, 4.11; 95% CI, 2.48–6.84; $P \leq 0.001$, respectively). The test for heterogeneity was nonsignificant ($I^2 = 0\%$) (Fig. 3). No publication bias was observed (Egger’s $P = 0.26$, Supplement Figure 2, http://links.lww.com/CIR/A20).

Severity of COVID-19
The data for d-dimer levels were available in 9 studies.19–25,27,28 The pooled mean d-dimer levels were significantly elevated in patients with severe COVID-19 infection (WMD, 0.54 mg/L; 95% CI, 0.28–0.8; $P \leq 0.001$; $I^2 = 90.74\%$) (Fig. 4A). No publication bias was observed (Egger’s $P = 0.13$, Supplement Figure 3, http://links.lww.com/CIR/A20). Meta-regression analysis showed a significant association between CAD, C-reactive protein, and severe COVID-19 disease, but the results were not significant for age, male sex, and
comorbidities (hypertension, DM, troponin levels) (Table 4; Fig. 4B and 4C).

The risk of developing severe disease was twofold higher in patients with a positive d-dimer level versus negative d-dimer level (40.74% vs 21.98%; RR, 2.04; 95% CI, 1.34–3.11; P ≤ 0.001; I² = 81.83%, respectively) (Fig. 5). No publication bias was observed (Egger’s P = 0.16; Supplement Figure 4, http://links.lww.com/CIR/A20). A sensitivity analysis was performed by removing 1 study at a time (n-1 analysis) to investigate the high heterogeneity. No significant change in the findings was observed with the sensitivity analysis.

DISCUSSION

Elevated d-dimer is one of the abnormal laboratory parameters found in patients with COVID-19 infection. d-dimer is the fibrin degradation product released upon cleavage of cross-linked fibrin by plasmin, often utilized in diagnosing disseminated intravascular coagulation in those with low and intermediate pretest probability for deep vein thrombosis (DVT) and pulmonary embolism (PE).29 Historically, the role of d-dimer is limited due to its nonspecificity, with elevated levels often seen with advanced age, African American race, female sex, active malignancy, surgery, pregnancy, immobility, cocaine use, connective tissue disorders, end-stage renal disease, and prior thromboembolic disease.30 More recently, d-dimer has been explored to identify patients thought to develop severe COVID-19 infection earlier in their course of illness. A previous meta-analysis comprising 4 studies demonstrated elevated d-dimer levels in patients with severe COVID-19 infection compared with those with the nonsevere disease.31 However, this meta-analysis was limited by a relatively small sample size, and it failed to answer the clinically relevant question regarding the prognostic value of d-dimer in predicting severe COVID-19 infection and mortality. Our meta-analysis comprising 18 studies evaluated the prognostic role of d-dimer in COVID-19-infected patients, and is the largest to date, to the best of our knowledge. The key findings of our pooled analysis are: (1) the d-dimer levels were higher in patients with severe COVID-19 infection and those who succumbed to death, compared with nonsevere disease and those who survived, respectively; (2) patients with elevated d-dimer levels were at an increased risk of developing severe COVID-19 infection and increased all-cause mortality compared with those with normal d-dimer levels.

Zhou et al13 reported that d-dimer levels >1 mg/L on admission in COVID-19-infected patients were independently associated with increased odds of mortality, a finding that echoes with our pooled analysis. Also, patients with advanced age, higher Sequential Organ Failure Assessment score, elevated troponin, and B-type natriuretic peptide have been associated with poor outcomes and mortality in COVID-19 infection.13,32,33 Furthermore, using a higher cutoff value of d-dimer (levels >2 mg/L) predicted in-hospital mortality even better, as noted by Zhang et al,17 with a sensitivity of 92.3% and a specificity of 83.3% after adjusting for age, gender, and comorbidities. Besides, studies have shown that rising d-dimer levels during the course of hospitalization were associated with worse long-term outcomes.12,13

The prognostic value of d-dimer, as seen in COVID-19 infection, has also been noted in sepsis and other infections (like pneumonia or influenza). Patients with sepsis who had elevated d-dimer levels on admission demonstrated a higher 28-day mortality.34 Likewise, elevated d-dimer levels may help predict severe community-acquired pneumonia.35 Elevated d-dimer was also noted in the 2009 novel influenza A (H1N1) infection among critically-ill patients and those who died.36 Other than infections, elevated d-dimer levels have been associated with adverse clinical outcomes in numerous cardiovascular conditions (like CAD and congestive heart failure).37,38

FIGURE 1. Flow diagram illustrating the systematic search of studies

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### TABLE 1. Baseline Characteristics of Studies Included in the Meta-Analysis Comparing COVID-19-Infected Patients Who Died Versus Patients Who Survived

| Study Name     | Study Type | Country     | Study Period          | Age (yr)     | Male | Groups   | N     | Diabetes | Hypertension | Coronary Artery Disease | Shock |
|----------------|------------|-------------|-----------------------|--------------|------|----------|-------|----------|--------------|-------------------------|-------|
| Zhang et al    | Retrospective | China       | January 12–March 15, 2020 | 62 (IQR 48–69) | 169  | Overall  | 343   | 47 (13.7%) | 76 (22.2%) | 19 (5.5%) | NR             |
| Wang et al     | Retrospective | China       | January 1–February 6, 2020 | 69 (IQR 65–76) | 166  | Survived | 274   | 43 (15.7%) | 106 (38.7%) | NR           | 5 (1.8%) |
| Tang et al     | Retrospective | China       | January 1–February 13, 2020 | 65.1 ± 12.0  | 268  | Nonsevere | 315   | NR       | NR           | NR           | NR            |
| Zhou et al     | Retrospective | China       | December 29, 2019–February 1, 2020 | 56 (IQR 46–67) | 119  | Survived | 137   | 19 (13.9%) | 32 (23.4%) | 2 (1.5%)   | NR           |
| Du et al       | Prospective | China       | December 25, 2019–February 7, 2020 | 57.6 ± 13.7  | 97   | Survived | 158   | 27 (17.1%) | 45 (28.5%) | NR          | NR           |
| Cao et al      | Retrospective | China       | January 3–February 1, 2020 | 54 (IQR 37–67) | 53   | Nonsevere | 85    | 5 (5.9%)  | 17 (20%)   | NR          | NR       |
| Hu et al       | Retrospective | China       | January 8–February 20, 2020 | 61 (range 23–91) | 166  | Nonsevere | 166   | 14 (8.4%) | 41 (24.8%) | NR          | NR       |
| Ji et al       | Prospective | China       | January 20–February 16, 2020 | 43.6 ± 17.1  | 31   | Nonsevere | 58    | 19 (32%)  | 38 (62%)   | NR          | NR       |
| Ma et al       | Retrospective | China       | January 21–March 2, 2020 | 48 (IQR 42.3–62.5) | 48   | Nonsevere | 48    | 14 (29.2%) | 22 (46.8%) | NR          | NR       |
| Hu et al       | Prospective | China       | January 8–February 20, 2020 | 61 (range 23–91) | 166  | Nonsevere | 166   | 14 (8.4%) | 41 (24.8%) | NR          | NR       |
| Wan et al      | Retrospective | China       | January 23–February 8, 2020 | 47 (IQR 36–55) | 72   | Nonsevere | 95    | 3 (3.2%)  | 9 (9.5%)   | NR          | 0 (0%)   |
| Guan et al     | Retrospective | China       | December 11, 2019–January 29, 2020 | 47 (IQR 35–58) | 637  | Nonsevere | 926   | 53 (5.7%) | 124 (13.4%) | 17 (1.8%)  | NR       |
| COVID-19 indicates coronavirus disease 2019; N, number; IQR, interquartile range; NR, not reported.

### TABLE 2. Baseline Characteristics of Studies Included in the Meta-Analysis Comparing Severe Versus Nonsevere COVID-19-Infected Patients

| Study Name     | Study Type | Country     | Study Period          | Age (yr)     | Male | Groups   | N     | Diabetes | Hypertension | Coronary Artery Disease | Shock |
|----------------|------------|-------------|-----------------------|--------------|------|----------|-------|----------|--------------|-------------------------|-------|
| Deng et al     | Retrospective | China       | January 6–February 20, 2020 | 65 (IQR 49–70.8) | 57   | Nonsevere | 45    | 5 (11.1%) | 12 (26.7%) | 4 (8.9%) | NR             |
| Chen et al     | Retrospective | China       | December–January 27, 2020 | 56 (IQR 50–65) | 17   | Nonsevere | 10    | 1 (10%)  | 1 (10%)      | 11 (16.4%) | NR             |
| Zhang et al    | Retrospective | China       | January 16–February 3, 2020 | 57 (range 25–87) | 71   | Nonsevere | 82    | 9 (11%)  | 20 (24.4%) | NR          | 1 (9.1%) |
| Qian et al     | Retrospective | China       | January 20–February 11, 2020 | 50 (IQR 36.5–57) | 37   | Nonsevere | 82    | 8 (13.8%) | 22 (37.9%) | NR          | 1 (0.9%) |
| Cai et al      | Retrospective | China       | January 11–February 9, 2020 | 47 (IQR 33–61) | 149  | Nonsevere | 240   | 19 (6.4%) | 38 (12.8%) | NR          | NR       |
| Ji et al       | Prospective | China       | January 20–February 16, 2020 | 43.6 ± 17.1  | 31   | Nonsevere | 34    | NR       | NR           | NR          | NR       |
| Lu et al       | Retrospective | China       | January 20–February 19, 2020 | NR           | NR   | Nonsevere | 243   | 15 (6.2%) | 42 (17.3%) | 10 (4.1%) | NR             |
| Ma et al       | Retrospective | China       | January 21–March 2, 2020 | 48 (IQR 42.3–62.5) | 48   | Nonsevere | 48    | 14 (29.2%) | 22 (46.8%) | NR          | NR       |
| Hu et al       | Retrospective | China       | January 8–February 20, 2020 | 61 (range 23–91) | 166  | Nonsevere | 166   | 14 (8.4%) | 41 (24.8%) | NR          | NR       |
| Wan et al      | Retrospective | China       | January 23–February 8, 2020 | 47 (IQR 36–55) | 72   | Nonsevere | 95    | 3 (3.2%)  | 9 (9.5%)   | NR          | 0 (0%)   |
| Guan et al     | Retrospective | China       | December 11, 2019–January 29, 2020 | 47 (IQR 35–58) | 637  | Nonsevere | 926   | 53 (5.7%) | 124 (13.4%) | 17 (1.8%)  | NR       |
| COVID-19 indicates coronavirus disease 2019; N, number; IQR, interquartile range; NR, not reported.
Nonetheless, in our analysis, patients who died as a result of COVID-19 infection were noted to have elevated d-dimer levels even after adjusting for age and comorbidities. However, no single cutoff value (both in COVID and non-COVID illnesses) has been identified to predict adverse outcomes consistently.

There has been evidence regarding an increased incidence of venous thromboembolic events (VTE), including DVT and PE, in patients with severe COVID-19 infection. One study proposed that d-dimer levels > 1.5 mg/L may help detect VTE events with a sensitivity of 85.0% and specificity of 88.5%; however, results should be interpreted with caution due to small sample size and lack of external validation. It remains unclear if this is a direct consequence of SARS-CoV-2 infection or a due to cytokine storm resulting in the systemic inflammatory response syndrome, as seen in other viral infections. A similar pattern of changes in coagulation cascade with increased prothrombotic state and incidences of DVT and PE were also noted with the coronavirus responsible for Middle Eastern Respiratory Syndrome (MERS-CoV) and SARS-CoV-1. The risk of VTE is generally high in critically-ill patients, but the risk appears to be higher in patients infected with SARS-CoV-2.

While hypercoagulability could be one of the reasons for elevated d-dimer levels in severe COVID-19 infection, these patients may also have several other reasons for d-dimer elevation, including renal dysfunction, disseminated intravascular coagulation, atrial fibrillation, stroke, acute coronary syndrome, infection, and acute upper gastrointestinal bleed, especially among those admitted to the ICU. Furthermore, d-dimer has low specificity to detect VTE in critically-ill patients. Thus, imaging studies to diagnose

**FIGURE 2.** d-Dimer levels. The Forest plot for pooled weighted mean difference in d-dimer levels in dead versus survived COVID-19 patients. COVID-19 indicates coronavirus disease 2019.

**TABLE 3.** Metaregression of Baseline Characteristics with Weighted Mean Difference in d-Dimer Levels in COVID-19 Patients—Dead Versus Survived

| Dead versus survived COVID-19 | Metaregression |  
| Weighted mean difference (95% CI) | Age | Male | Hypertension | Diabetes | CAD | Troponin |
|---|---|---|---|---|---|---|
| d-dimer levels | 6.13 (4.16–8.11), P < 0.001 | β = 0.02, P = 0.91 | β = 0.05, P = 0.62 | β = -0.002, P = 0.98 | β = 0.15, P = 0.82 | β = -0.12, P = 0.25 | β = 201.41, P = 0.53 |

COVID-19 indicates coronavirus disease 2019; CI, confidence interval; CAD, coronary artery disease.

**FIGURE 3.** All-cause mortality. The Forest plot shows the outcomes of the individual trials as well as the aggregate.
FIGURE 4. Disease severity. A, The Forest plot for pooled weighted mean difference in d-dimer levels in severe versus nonsevere COVID-19 patients, followed by random-effects meta-regression analysis plots depicting the relationship between weighted mean differences in d-dimer levels (on y-axis) and (B) CAD and (C) CRP. Each included study is represented by a circle, the size of which is proportional to its respective weight in the analysis. The line indicates the predicted effects (regression line). There was significant association between CAD ($\beta = 0.8$, $P = 0.02$), and CRP levels ($\beta = 0.02$, $P = 0.03$) and mean differences in d-dimer levels. COVID-19 indicates coronavirus disease 2019; CAD, coronary artery disease; CRP, C-reactive protein.

TABLE 4. Metaregression of Baseline Characteristics with Weighted Mean Difference in d-Dimer Levels in Severe Versus Nonsevere COVID-19-Infected Patients

| Metaregression | Weighted mean difference and 95% CI |
|----------------|-------------------------------------|
| Age            | $\beta = 0.03$, $P = 0.31$          |
| Male           | $\beta = 0.008$, $P = 0.68$         |
| Hypertension   | $\beta = 0.03$, $P = 0.2$           |
| Diabetes       | $\beta = -0.01$, $P = 0.84$         |
| CAD*           | $\beta = 0.8$, $P = 0.02$           |
| CRP*           | $\beta = 0.02$, $P = 0.03$          |
| Troponin       | $\beta = 105.63$, $P = 0.06$        |

COVID-19 indicates coronavirus disease 2019; CI, confidence interval; CAD, coronary artery disease; CRP, C-reactive protein.

*Indicates statistically significant value.

FIGURE 5. The Forest plot demonstrating the risk ratio of positive d-dimer with severity.
DVT or PE should only be pursued if clinically warranted. 40 Per-
haps, empirically treating all COVID-19 patients with intermediate or full (therapeutic) doses of anticoagulation to prevent microvas-
cular thrombosis 44,46 might be beneficial (provided a thorough risk-
benefit assessment is performed given these patients are also at-risk of
spontaneous bleeding). However, our study was not designed to
assess this difference.

Our study has a few important limitations. First, all studies
included in our meta-analysis were from China, while currently the
United States and Europe have the majority of COVID-19 cases.
However, the preliminary reports from the United States and Europe
have shown similar trends in COVID-19 infection in terms of clinical
presentation and outcomes. 4,44 Our pooled analysis provides the
best available data regarding trends of D-dimer levels in patients with
COVID-19 infection, and the likelihood of developing severe infec-
tion or mortality in patients with elevated D-dimer levels. Second, all
studies included in our analysis were either prospective or retrospec-
tive reports, which is currently the best available evidence and there-
fore, subject to potential confounding and publication bias. Third,
high heterogeneity was observed between studies in our pooled
analysis. Fourth, details on trends of D-dimer over the course of hos-
pitalization were not available. Fifth, the normal reference range
of D-dimer varied slightly among studies, and details regarding the
assays used to measure D-dimer were not available in most studies.
Sixth, trends in D-dimer levels for COVID-19 patients never hospo-
tialized remain unknown. Finally, patient-level data to perform addi-
tional detailed analysis were not available.

CONCLUSIONS

Our meta-analysis demonstrates that patients with COVID-19
presenting with elevated D-dimer levels have an increased risk of se-
vere disease and mortality.

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