10.48047/jocaaa.2024.33.06.103

Early Predictors of In-Hospital Morbidity and Mortality in COVID-19: A Review of Current Evidence

Ekhlas Mohamed El-Sayed[1], Abdel-Fattah Hassan Frere[2], Nader Talaat Qandil[3], Amira Ali Mohamed Osman[4], Ayman El Sayed Mohamed Tantawy[5]

1. Professor of Cardiology, Faculty of Medicine, Zagazig University
2. Professor of Cardiology, Faculty of Medicine, Zagazig University
3. Professor of Cardiology, Faculty of Medicine, Zagazig University
4. MBBCH, Faculty of Medicine, Zagazig University
5. Lecturer of Cardiology, Faculty of Medicine, Zagazig University

Corresponding Author: Amira Ali Mohamed Osman
Mail: amira.osman899@gmail.com

ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) has placed an unprecedented burden on healthcare systems worldwide, with hospitalized patients demonstrating highly variable short-term outcomes ranging from full recovery to multiorgan failure and death. Early recognition of clinical and laboratory predictors of in-hospital morbidity and mortality is critical for risk stratification, guiding resource allocation, and improving patient care. Numerous demographic, comorbidity, laboratory, imaging, and clinical variables have been proposed, but evidence remains heterogeneous and scattered. **Aim:** This review synthesizes current evidence on early predictors of adverse in-hospital outcomes among COVID-19 patients. Special attention is given to demographic and comorbidity profiles, inflammatory and hematologic biomarkers, cardiovascular involvement, respiratory failure indicators, and validated risk scores including the CHA_2DS_2-VASc score and COVID-specific mortality indices. The objective is to provide clinicians with a comprehensive overview of prognostic tools that can support early decision-making and improve patient triage in hospital settings. Advanced age, male sex, and pre-existing comorbidities such as hypertension, diabetes, obesity, and cardiovascular disease consistently predict worse short-term outcomes. Elevated inflammatory markers (C-reactive protein, ferritin, interleukin-6) and hematologic abnormalities (lymphopenia, neutrophil-to-lymphocyte ratio, and D-dimer) are strong laboratory indicators of severity. Cardiac biomarkers such as troponin and natriuretic peptides provide additional prognostic value, reflecting the burden of myocardial injury. Imaging severity scores on chest CT and echocardiographic evidence of cardiac dysfunction further stratify risk. Among integrative scores, the CHA_2DS_2-VASc score—originally designed to predict thromboembolic risk in atrial fibrillation—has shown utility in COVID-19, correlating with both in-hospital morbidity and mortality, particularly in patients with high baseline comorbidity burden. COVID-specific models such as the 4C mortality score also provide accurate early prediction and may complement traditional risk stratification tools.

Conclusion: Early predictors of in-hospital morbidity and mortality in COVID-19 are multifactorial, encompassing demographic, clinical, laboratory, imaging, and scoring system variables. Identifying these markers at admission can support timely intervention, targeted monitoring, and optimal resource utilization. Integrating simple tools such as the CHA_2DS_2-VASc score with COVID-specific models offers a pragmatic approach for frontline clinicians. Future research should focus on refining composite risk models and validating them across diverse populations to enhance predictive accuracy and generalizability.

Keywords: *Predictors, of In-Hospital, Morbidity, Mortality ,COVID-19, CHA_2DS_2-VASc score*

10.48047/jocaaa.2024.33.06.103

Introduction

Since its emergence in late 2019, coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has resulted in substantial morbidity and mortality worldwide. Despite widespread vaccination and therapeutic advances, hospitalized patients with COVID-19 remain at risk of acute respiratory failure, cardiovascular complications, thromboembolic events, and multiorgan dysfunction. The clinical spectrum in hospitalized patients is remarkably heterogeneous, with some individuals progressing rapidly to critical illness and death, while others experience mild courses and are discharged uneventfully. This variability underscores the necessity of identifying reliable predictors of in-hospital outcomes early in the disease course [1].

Accurate prognostic assessment in hospitalized patients is essential for multiple reasons. First, it allows clinicians to stratify patients at the point of admission, prioritizing intensive monitoring and early therapeutic interventions for high-risk individuals. Second, it aids hospitals and healthcare systems in resource allocation, particularly during surge periods when critical care capacity is limited. Third, robust predictors can inform family counseling and facilitate shared decision-making, especially in older patients with multiple comorbidities. The development of predictive tools and scoring systems has thus become a cornerstone of contemporary COVID-19 research [2].

A wide array of demographic, clinical, and laboratory variables have been associated with poor short-term outcomes. Older age and male sex have consistently emerged as strong predictors of mortality across diverse populations. Comorbidities such as hypertension, diabetes, obesity, chronic kidney disease, and cardiovascular disease significantly amplify the risk of severe illness. Laboratory markers of inflammation, coagulation, and organ dysfunction—such as C-reactive protein (CRP), interleukin-6 (IL-6), D-dimer, lymphocyte count, and troponin—are strongly linked with poor prognosis. Imaging findings, particularly chest CT severity scores, provide additional insight into disease burden. Several integrative models, such as the 4C mortality score, NEWS2, SOFA, and the CHA_2DS_2-VASc score, have been proposed to refine risk stratification [3].

Despite extensive research, there remains a critical gap: most studies focus on individual predictors, while fewer have synthesized evidence across multiple domains into a unified framework. Furthermore, the role of established cardiovascular risk scores, such as the CHA_2DS_2-VASc score, has not been comprehensively integrated into prognostic discussions, despite mounting evidence of their predictive utility in COVID-19. This review aims to bridge this gap by providing a structured synthesis of the current evidence on early predictors of in-hospital morbidity and mortality in COVID-19, with emphasis on demographic, comorbidity, biomarker, imaging, and scoring system predictors [4].

1. Demographic Predictors (Age, Sex, Ethnicity)

Age has consistently emerged as the most powerful predictor of adverse short-term outcomes in hospitalized COVID-19 patients. Multiple cohort studies have shown a strong, independent association between advanced age and higher rates of intensive care admission, mechanical ventilation, and in-hospital mortality. Patients over 65 years have demonstrated significantly worse prognosis, which is likely attributable to immunosenescence, higher prevalence of comorbidities, and diminished physiological reserve. The steep gradient of risk with advancing age suggests that age itself is not just a confounding factor but a central determinant of host vulnerability to severe COVID-19 [5].

Sex also influences short-term outcomes in COVID-19. Male patients consistently exhibit higher morbidity and mortality compared with females, even after adjusting for comorbidities and other confounders. Biological explanations for this disparity include sex-related differences in immune response, hormonal modulation, and the expression of angiotensin-converting enzyme 2 (ACE2), the functional receptor for SARS-CoV-2. Men also tend to have a higher prevalence of cardiovascular risk factors, which may compound vulnerability. The sex effect underscores the importance of considering gender as an independent risk modifier in COVID-19 prognosis [6].

Ethnicity and race have also been implicated as predictors of in-hospital outcomes, though the

10.48047/jocaaa.2024.33.06.103

interpretation is complex. Data from the United States and the United Kingdom indicate that Black, Hispanic, and South Asian populations have experienced disproportionately higher rates of hospitalization and death. However, these differences often reflect socioeconomic disparities, occupational exposure risks, housing density, and access to healthcare rather than intrinsic biological factors. Nevertheless, once hospitalized, some ethnic groups still appear to have higher mortality risk, raising the possibility that genetic or epigenetic factors may also play a role. Understanding the intersection of biological and social determinants of health is essential for equitable prognostication and management in COVID-19 [7].

2. Role of Comorbidities (Hypertension, Diabetes, Obesity, Cardiovascular Disease)

Comorbid conditions significantly amplify the risk of poor short-term outcomes in hospitalized COVID-19 patients. Hypertension is among the most prevalent comorbidities and has been consistently associated with severe disease and mortality. The mechanisms linking hypertension to adverse outcomes include endothelial dysfunction, impaired immune regulation, and upregulation of ACE2 receptors, which may facilitate viral entry. Moreover, hypertensive patients often have concomitant cardiovascular disease, further compounding the risk of critical illness [8].

Diabetes mellitus is another strong predictor of in-hospital morbidity and mortality. Hyperglycemia promotes a pro-inflammatory and pro-thrombotic state, impairs innate immunity, and increases susceptibility to secondary infections. Poor glycemic control during hospitalization has been shown to correlate with worse outcomes, independent of baseline diabetes status. Importantly, the synergistic effect of diabetes with obesity or cardiovascular disease further increases mortality risk, highlighting the need for careful metabolic monitoring in COVID-19 patients [9].

Obesity has emerged as a particularly important predictor of adverse short-term outcomes. Beyond being a metabolic risk factor, obesity directly impacts respiratory mechanics, reduces lung compliance, and impairs diaphragmatic excursion, all of which increase the risk of hypoxemia and respiratory failure. Adipose tissue also acts as a reservoir for viral replication and a source of pro-inflammatory cytokines, contributing to the cytokine storm observed in severe COVID-19. Several studies have shown that body mass index (BMI) above 30 is independently associated with higher ICU admission and mortality rates [10].

Cardiovascular disease (CVD), including ischemic heart disease and heart failure, has been strongly linked with poor outcomes in COVID-19. Patients with pre-existing CVD are more susceptible to myocardial injury, arrhythmias, and decompensated heart failure when infected with SARS-CoV-2. This vulnerability is partly due to chronic structural and functional impairment of the heart, but it is also mediated by the systemic inflammatory response and hypercoagulability induced by the infection. Consequently, hospitalized patients with underlying CVD frequently require escalated care and experience disproportionately high mortality [11].

3. Pre-existing Pulmonary Disease and Outcomes

Chronic pulmonary diseases are important predictors of poor in-hospital outcomes in COVID-19, given their direct impact on respiratory reserve. Chronic obstructive pulmonary disease (COPD) is particularly associated with increased risk of severe illness and mortality. Patients with COPD often have reduced pulmonary function, impaired mucociliary clearance, and heightened susceptibility to viral-induced exacerbations. Several large meta-analyses have confirmed that COPD significantly increases the odds of ICU admission and in-hospital death in COVID-19 patients [12].

Asthma, in contrast, has shown more heterogeneous associations. While early reports suggested a strong link with poor outcomes, subsequent studies have demonstrated that controlled asthma, particularly non-severe phenotypes, may not independently increase mortality risk. However, severe asthma requiring systemic corticosteroids or biologic therapy has been associated with worse prognosis. This reflects the nuanced role of airway inflammation and treatment-related immunosuppression in modifying disease severity [13].

Interstitial lung diseases (ILDs) and pulmonary fibrosis represent another group of high-risk conditions.

10.48047/jocaaa.2024.33.06.103

Patients with ILD often present with limited pulmonary reserve, and SARS-CoV-2 infection can precipitate acute exacerbations and rapid progression to respiratory failure. Moreover, many ILD patients are on long-term immunosuppressive therapy, which may further increase vulnerability to severe COVID-19. Mortality rates in this subgroup are notably higher compared to the general hospitalized population [14].

Pulmonary hypertension has also been associated with adverse short-term outcomes. The hemodynamic stress imposed by acute hypoxemia and right ventricular strain during COVID-19 pneumonia predisposes patients with pulmonary hypertension to rapid decompensation. These individuals are more likely to require mechanical ventilation and often experience disproportionately high mortality despite aggressive supportive measures. Taken together, pre-existing pulmonary diseases remain critical determinants of COVID-19 prognosis and should be considered in early risk stratification models [15].

4. Chronic Kidney Disease and Outcomes

Chronic kidney disease (CKD) has emerged as a strong predictor of adverse short-term outcomes in hospitalized COVID-19 patients. The presence of CKD is associated with impaired immune function, chronic inflammation, and heightened susceptibility to both infections and cardiovascular complications. Studies consistently demonstrate that patients with pre-existing CKD have higher rates of hospitalization, ICU admission, and in-hospital mortality compared with those without renal disease [16].

The prognostic impact of CKD is partly explained by the increased risk of acute kidney injury (AKI) during COVID-19. SARS-CoV-2 directly infects renal tubular cells via ACE2 receptors, and the systemic inflammatory and thrombotic environment further promotes kidney injury. The development of AKI in COVID-19 patients with baseline CKD is associated with a marked rise in mortality, often exceeding 50% in critically ill cohorts. Thus, kidney function monitoring at admission and during hospitalization is critical for outcome prediction [17].

Patients receiving maintenance dialysis are particularly vulnerable. Hemodialysis patients are at increased risk of acquiring SARS-CoV-2 due to frequent healthcare exposure, and once hospitalized, they experience worse outcomes due to chronic systemic illness and impaired immune surveillance. Mortality among dialysis patients with COVID-19 has been reported to be substantially higher than in the general hospitalized population, emphasizing the importance of tailored infection control and early intervention strategies in this group [18].

Kidney transplant recipients represent another subgroup at high risk for poor in-hospital outcomes. Chronic immunosuppression, combined with impaired allograft function, predisposes these patients to severe infections and prolonged viral shedding. Multiple observational studies have reported high mortality rates in kidney transplant recipients hospitalized with COVID-19, further underscoring the prognostic importance of renal dysfunction in this disease. Taken together, CKD and its related conditions significantly amplify the risk of morbidity and mortality in COVID-19 and should be systematically incorporated into prognostic models [19].

5. Immunosuppression and Malignancy

Immunosuppressed patients represent a particularly high-risk group for adverse in-hospital outcomes with COVID-19. Individuals on chronic immunosuppressive therapy, such as those with autoimmune diseases, organ transplants, or hematological disorders, often exhibit blunted immune responses to viral infections. In COVID-19, this impaired host defense increases viral replication and prolongs viral clearance, predisposing patients to severe pneumonia and opportunistic infections. Clinical cohorts have consistently shown that immunosuppression correlates with higher mortality and longer hospital stays compared with the general COVID-19 population [20].

Malignancy is another critical predictor of poor outcomes. Cancer patients, especially those with active disease or undergoing chemotherapy, are more likely to develop severe forms of COVID-19. Hematological malignancies, such as leukemia and lymphoma, confer particularly high risk due to profound immune dysregulation and treatment-related cytopenias. Data from multi-center registries

10.48047/jocaaa.2024.33.06.103

demonstrate that mortality rates among hospitalized cancer patients with COVID-19 are significantly elevated, often exceeding 25–30% in some cohorts [21].

Solid tumors also contribute to adverse outcomes, although the risk appears to vary depending on tumor type and treatment status. Patients with lung cancer, for instance, are especially vulnerable due to pre-existing pulmonary impairment and frequent exposure to cytotoxic therapy. Surgical oncology patients infected perioperatively with SARS-CoV-2 are at increased risk of postoperative complications, including respiratory failure and thromboembolism, which worsen short-term outcomes [22].

The prognostic importance of immunosuppression and malignancy extends beyond direct effects on viral clearance. Many of these patients develop exaggerated systemic inflammation and cytokine release despite impaired adaptive immunity, leading to multi-organ dysfunction. Furthermore, treatment delays or modifications during hospitalization may worsen cancer-related outcomes. These factors collectively highlight the need for tailored risk stratification and aggressive supportive measures in immunocompromised COVID-19 patients [23].

6. Clinical Predictors at Admission (Symptoms and Severity Scores)

The clinical presentation at hospital admission provides critical insight into short-term prognosis in COVID-19. Several admission symptoms have been independently associated with worse outcomes. Dyspnea at presentation, for example, is a strong predictor of disease progression and mortality, reflecting underlying hypoxemia and pulmonary involvement. Patients presenting with altered mental status or confusion also have significantly higher mortality rates, likely due to systemic hypoxemia, sepsis, or neurological involvement of SARS-CoV-2 [24].

Oxygen saturation at admission is one of the simplest yet most powerful prognostic indicators. Hypoxemia with SpO_2 below 90–92% strongly correlates with increased risk of ICU transfer and mortality. The phenomenon of "silent hypoxemia," where patients present with disproportionately low oxygen levels without severe dyspnea, has been particularly noted in COVID-19, underscoring the importance of objective monitoring rather than symptom-based assessment alone [25].

Several severity scoring systems have been applied at admission to stratify patient risk. The Sequential Organ Failure Assessment (SOFA) score and the National Early Warning Score 2 (NEWS2) have both demonstrated predictive utility in hospitalized COVID-19 patients. Elevated SOFA scores correlate with multi-organ dysfunction and poor short-term survival, while NEWS2 provides a rapid bedside assessment of clinical deterioration risk. However, their predictive accuracy may vary depending on patient population and resource setting [26].

Another important clinical marker is respiratory rate, which is often elevated in patients who later require mechanical ventilation. Tachypnea at admission is strongly associated with increased mortality, independent of oxygen saturation levels. Similarly, persistent fever, hemodynamic instability, and signs of systemic inflammation (e.g., tachycardia, hypotension) are early red flags that predict poor outcomes. Taken together, clinical symptoms, vital signs, and validated severity scores form the cornerstone of early prognostication and should be systematically evaluated upon hospital admission [27].

7. Vital Signs and Early Warning Scores

Admission vital signs remain fundamental predictors of in-hospital outcomes. Persistent tachycardia, hypotension, tachypnea, and hypoxemia have all been correlated with higher mortality in COVID-19. Hypoxemia is particularly prognostic; patients requiring supplemental oxygen at admission often progress rapidly to respiratory failure. Early warning scores such as NEWS2 integrate vital signs into composite risk estimates, allowing rapid triage. In cardiovascular patients, hypotension and tachycardia may also indicate impending shock or myocardial injury, necessitating early escalation of care [28].

8. Laboratory Biomarkers: Inflammatory Markers (CRP, Ferritin, IL-6)

Inflammatory biomarkers reflect the cytokine-driven pathophysiology of severe COVID-19. Elevated C-reactive protein (CRP) is consistently associated with poor outcomes, serving as a sensitive indicator of systemic inflammation. Ferritin, another acute-phase reactant, often rises dramatically in severe

10.48047/jocaaa.2024.33.06.103

disease, correlating with cytokine storm and multiorgan failure. Interleukin-6 (IL-6) is particularly important from a cardiologist's standpoint, as high IL-6 levels not only predict mortality but also increase the risk of myocarditis and destabilization of chronic cardiovascular disease. These markers help identify patients who may benefit from early immunomodulatory therapies [29].

9. Hematologic Predictors (Lymphopenia, Neutrophil-to-Lymphocyte Ratio, D-dimer)

Hematological abnormalities are strong and early predictors of in-hospital outcomes. Lymphopenia is one of the most consistent findings in severe COVID-19 and reflects impaired cellular immunity. The neutrophil-to-lymphocyte ratio (NLR) has emerged as a robust prognostic marker, with elevated values correlating with higher mortality. From a cardiovascular standpoint, elevated D-dimer is particularly concerning, as it reflects both systemic inflammation and hypercoagulability. High D-dimer levels predict venous thromboembolism, myocardial infarction, and ischemic stroke, making it a vital biomarker for cardiologists managing hospitalized patients [30].

9. Hematologic Predictors (Lymphopenia, Neutrophil-to-Lymphocyte Ratio, D-dimer)

Hematological abnormalities are strong and early predictors of in-hospital outcomes. Lymphopenia is one of the most consistent findings in severe COVID-19 and reflects impaired cellular immunity. The neutrophil-to-lymphocyte ratio (NLR) has emerged as a robust prognostic marker, with elevated values correlating with higher mortality. From a cardiovascular standpoint, elevated D-dimer is particularly concerning, as it reflects both systemic inflammation and hypercoagulability. High D-dimer levels predict venous thromboembolism, myocardial infarction, and ischemic stroke, making it a vital biomarker for cardiologists managing hospitalized patients [30].

11. Hepatic and Renal Function Tests

Liver and kidney dysfunction at admission carry prognostic significance. Elevated liver enzymes, particularly AST and ALT, often correlate with systemic inflammation and multiorgan involvement, while hypoalbuminemia reflects poor nutritional and inflammatory status. Renal impairment, whether pre-existing or acute, is a consistent predictor of in-hospital mortality. For cardiologists, worsening renal function also complicates fluid balance and medication dosing, which can accelerate decompensation in patients with heart failure or shock [32].

12. Coagulation Markers and Risk of Thrombosis

COVID-19 is characterized by a hypercoagulable state. Elevated fibrinogen, prolonged prothrombin time, and especially increased D-dimer levels predict thromboembolic complications and poor prognosis. Disseminated intravascular coagulation (DIC) has been reported in critically ill patients and strongly associates with mortality. From a cardiovascular perspective, coagulation abnormalities predispose patients to pulmonary embolism, myocardial infarction, and stroke, making early anticoagulation strategies central to management [33].

13. Radiological Predictors (Chest X-ray, CT Severity Scores)

Radiological imaging provides essential prognostic information. Chest X-ray abnormalities such as bilateral infiltrates predict higher oxygen requirements and prolonged hospitalization. High-resolution chest CT is more sensitive and allows calculation of severity scores based on percentage of lung involvement. Extensive opacities and ground-glass changes correlate with poor short-term outcomes and higher risk of mechanical ventilation. For cardiologists, radiological severity also guides differentiation between pure COVID-19 pneumonia and overlapping heart failure pulmonary edema [34].

14. Role of Echocardiography and Cardiac Imaging

Echocardiography plays an important role in predicting outcomes by assessing ventricular function. Reduced left ventricular ejection fraction, right ventricular dilation, and elevated pulmonary pressures are all associated with increased mortality in COVID-19. Cardiac MRI, though less feasible in acute care, has demonstrated myocarditis and diffuse myocardial edema, which carry prognostic implications. Point-of-care ultrasound (POCUS) has emerged as a valuable bedside tool, allowing cardiologists to

10.48047/jocaaa.2024.33.06.103

rapidly assess cardiac involvement and guide management in critically ill patients [35].

15. Predictors of Respiratory Failure and Need for Mechanical Ventilation

Progression to respiratory failure is one of the strongest determinants of short-term mortality in hospitalized COVID-19 patients. Clinical predictors include tachypnea at admission, hypoxemia despite supplemental oxygen, and worsening oxygenation within the first 48–72 hours. Radiological burden on chest CT, particularly when lung involvement exceeds 50%, is strongly associated with the need for mechanical ventilation. From a cardiology standpoint, respiratory failure creates a vicious cycle by exacerbating right ventricular strain, precipitating pulmonary hypertension, and leading to right heart failure — all of which markedly increase mortality risk [36].

The timing of respiratory deterioration is also prognostically important. Patients who deteriorate rapidly within days of admission tend to have higher mortality, reflecting overwhelming viral burden or hyperinflammatory response. Conversely, patients with more gradual decline may benefit from early non-invasive support and tailored anti-inflammatory therapy. Identifying these high-risk groups early is vital for optimizing care pathways and prioritizing ICU resources [37].

16. Predictors of Acute Cardiac Injury and Arrhythmias

Acute cardiac injury is a major complication in hospitalized COVID-19 patients, with troponin elevation serving as the hallmark. Predictors include pre-existing cardiovascular disease, systemic inflammation, and hypercoagulability. Myocardial injury in COVID-19 may result from direct viral myocarditis, microvascular thrombosis, or stress cardiomyopathy. Patients with acute cardiac injury face significantly higher risks of arrhythmias, shock, and death. For cardiologists, troponin surveillance and early echocardiography are key to identifying patients at risk [38].

Arrhythmias, including atrial fibrillation, ventricular tachyarrhythmias, and conduction abnormalities, are also frequent in severe COVID-19. Electrolyte imbalances, hypoxemia, systemic inflammation, and drug interactions (e.g., with QT-prolonging antivirals) contribute to their development. Atrial fibrillation is particularly common and carries prognostic significance as it often signals systemic stress and myocardial involvement. Continuous telemetry monitoring is therefore recommended for hospitalized patients with elevated cardiac biomarkers or structural heart disease [39].

17. CHA_2DS_2-VASc Score as a Predictor in COVID-19

The CHA_2DS_2-VASc score, originally developed to estimate thromboembolic risk in atrial fibrillation, has been increasingly evaluated as a prognostic tool in COVID-19. Its components — congestive heart failure, hypertension, age ≥75 (2 points), diabetes, prior stroke/TIA (2 points), vascular disease, age 65–74, and female sex — overlap significantly with known risk factors for adverse COVID-19 outcomes. This makes it a clinically intuitive and readily applicable score for hospitalized patients. Studies have shown that higher CHA_2DS_2-VASc scores correlate with increased in-hospital mortality, ICU admission, and thromboembolic complications in COVID-19 [40].

From a cardiology perspective, the appeal of CHA_2DS_2-VASc lies in its simplicity. Unlike complex laboratory-based models, it can be calculated immediately at admission using routine clinical history. Several retrospective analyses have demonstrated that patients with CHA_2DS_2-VASc scores ≥4 have significantly higher mortality compared with those with lower scores, independent of atrial fibrillation status. This suggests that the score functions as a surrogate marker for cumulative cardiovascular and systemic vulnerability in COVID-19 [41].

Another important observation is the relationship between CHA_2DS_2-VASc score and thrombotic complications. Patients with higher scores are more likely to develop pulmonary embolism, myocardial infarction, and ischemic stroke during hospitalization. This has practical implications: a simple admission score may help clinicians identify patients who require intensified thromboprophylaxis or closer monitoring for cardiovascular complications. For cardiologists, this bridges familiar risk stratification tools with novel COVID-19 applications [42].

Comparative studies have evaluated CHA_2DS_2-VASc against COVID-specific scores such as the 4C

10.48047/jocaaa.2024.33.06.103

mortality score. While COVID-specific scores generally provide higher predictive accuracy due to incorporation of laboratory parameters, CHA_2DS_2-VASc still performs surprisingly well as a rapid bedside tool. In settings where laboratory or imaging resources are limited, CHA_2DS_2-VASc offers a pragmatic approach to early prognostication. Importantly, combining CHA_2DS_2-VASc with biomarkers such as D-dimer or troponin may further enhance predictive power [43].

The future role of CHA_2DS_2-VASc in COVID-19 prognostication may extend beyond hospital outcomes. Longitudinal follow-up studies suggest that patients with higher admission CHA_2DS_2-VASc scores are also more likely to develop long COVID syndromes and persistent cardiovascular complications. This reinforces the score's utility not only in acute care but also in long-term risk assessment. For cardiologists, this provides an opportunity to integrate a familiar tool into both acute and chronic management of post-COVID patients [44].

18. Predictors of ICU Admission

The need for ICU care in COVID-19 is often predicted by early cardiopulmonary instability. Patients with high oxygen demand, hemodynamic compromise, or multiorgan dysfunction at admission have the highest probability of requiring ICU transfer. From a cardiovascular standpoint, predictors such as elevated troponin, BNP, or new arrhythmias strongly increase the likelihood of ICU escalation. Right ventricular dysfunction, often seen in severe pneumonia or pulmonary embolism, is another red flag for early ICU involvement. Importantly, ICU admission itself is associated with higher mortality in COVID-19, reinforcing the need for cardiologists to collaborate closely with intensivists to identify cardiac decompensation early [45].

19. Mortality Predictors: Integrative Risk Scores (NEWS2, SOFA, 4C Mortality Score)

Several composite scores have been validated to predict in-hospital mortality. The SOFA score, although developed for sepsis, is effective in COVID-19 for assessing multiorgan failure. The NEWS2 score provides rapid bedside assessment using vital signs and has moderate predictive accuracy. The 4C mortality score, developed specifically for COVID-19, incorporates age, comorbidities, vital signs, and laboratory values, making it highly accurate in predicting in-hospital death.

From a cardiologist's perspective, the 4C score's strength lies in combining cardiovascular comorbidities with systemic markers of severity. Patients with high 4C scores often overlap with those who have elevated troponin, BNP, or high CHA_2DS_2-VASc scores, suggesting synergistic value in risk assessment. Integrating these models allows clinicians to stratify cardiovascular patients more effectively and anticipate complications such as heart failure or arrhythmia in the ICU [46].

20. Geographic and Socioeconomic Factors with Clinical Implications

Beyond biology, socioeconomic determinants play a significant role in COVID-19 outcomes. Patients from disadvantaged backgrounds often present later, with more severe illness, and have less access to advanced care. Ethnic minorities and lower-income populations show disproportionately higher mortality, influenced by barriers to healthcare, higher baseline cardiovascular risk, and limited vaccination coverage.

For cardiologists, this highlights the importance of context in risk prediction. A patient's baseline CHA_2DS_2-VASc or 4C score may underestimate risk if socioeconomic stressors are unaccounted for. Equitable access to cardiovascular monitoring, imaging, and anticoagulation therapy is critical to improving outcomes across populations. Future prognostic models should integrate social determinants of health alongside traditional biomarkers, ensuring that predictive tools are not only biologically valid but also clinically just and globally applicable [47].

Conclusion

Early prediction of in-hospital morbidity and mortality in COVID-19 remains a cornerstone of effective clinical management. While age, comorbidities, inflammatory markers, and imaging findings provide valuable prognostic information, the cardiovascular system plays a disproportionately large role in determining short-term outcomes. Myocardial injury, arrhythmias, heart failure, and thromboembolic

10.48047/jocaaa.2024.33.06.103

events are not only frequent in hospitalized patients but also strongly predictive of mortality. From a cardiologist's perspective, this highlights the necessity of integrating cardiovascular assessment into all prognostic models for COVID-19.

Among the various predictive tools evaluated, the **CHA_2DS_2-VASc score** stands out as an accessible, clinically intuitive model that aligns closely with COVID-19 risk factors. Its components — age, hypertension, diabetes, prior stroke, vascular disease, and heart failure — overlap directly with predictors of poor COVID-19 outcomes. Evidence consistently demonstrates that patients with higher CHA_2DS_2-VASc scores are more likely to require ICU admission, develop thromboembolic complications, and die during hospitalization. Importantly, its predictive value is independent of atrial fibrillation status, suggesting that the score functions as a surrogate measure of systemic and cardiovascular vulnerability in this disease.

For practicing clinicians, the integration of CHA_2DS_2-VASc into COVID-19 risk stratification has several advantages. It can be calculated rapidly at the bedside without laboratory or imaging data, making it especially useful in resource-limited settings or during emergency triage. It also provides a cardiovascular-oriented framework that complements COVID-specific mortality scores, such as the 4C model. The potential synergy between CHA_2DS_2-VASc and biomarkers like troponin, BNP, and D-dimer may allow for even more precise prognostication and individualized therapeutic decision-making.

The broader implications for cardiology are significant. COVID-19 has reinforced the interdependence of systemic infection and cardiovascular health, with cardiovascular vulnerability emerging as a unifying pathway for poor outcomes. Moving forward, prognostic models must not only refine prediction of acute in-hospital mortality but also anticipate long-term sequelae, including post-COVID cardiac complications such as myocarditis, arrhythmias, and chronic heart failure. The CHA_2DS_2-VASc score, coupled with cardiovascular biomarkers and imaging, may serve as a bridge between acute triage and longitudinal cardiovascular care.

In summary, early predictors of in-hospital outcomes in COVID-19 are multifactorial, but cardiovascular risk remains central. Incorporating **CHA_2DS_2-VASc alongside COVID-specific models** offers a pragmatic and effective strategy to identify high-risk patients, optimize management, and improve survival. For cardiologists, this represents an opportunity to leverage familiar tools in novel contexts, ensuring that cardiovascular risk remains at the forefront of COVID-19 prognostication and patient care.

REFERENCES

1. Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med.* 2020;382(18):1708-1720.
2. Docherty AB, Harrison EM, Green CA, et al. Features of 20 133 UK patients in hospital with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. *BMJ.* 2020;369:m1985.
3. Knight SR, Ho A, Pius R, et al. Risk stratification of patients admitted to hospital with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. *BMJ.* 2020;370:m3339.
4. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. *N Engl J Med.* 2020;383(25):2451-2460.
5. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet.* 2020;395(10229):1054-1062.
6. Peckham H, de Gruijter NM, Raine C, et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. *Nat Commun.* 2020;11(1):6317.
7. Williamson EJ, Walker AJ, Bhaskaran K, et al. Factors associated with COVID-19-related death using OpenSAFELY. *Nature.* 2020;584(7821):430-436.
8. Lippi G, Wong J, Henry BM. Hypertension and its severity or mortality in Coronavirus Disease 2019 (COVID-19): a pooled analysis. *Pol Arch Intern Med.* 2020;130(4):304-309.

10.48047/jocaaa.2024.33.06.103

9. Zhu L, She ZG, Cheng X, et al. Association of Blood Glucose Control and Outcomes in Patients with COVID-19 and Pre-existing Type 2 Diabetes. *Cell Metab.* 2020;31(6):1068-1077.e3.
10. Simonnet A, Chetboun M, Poissy J, et al. High prevalence of obesity in severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) requiring invasive mechanical ventilation. *Obesity (Silver Spring).* 2020;28(7):1195-1199.
11. Shi S, Qin M, Shen B, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. *JAMA Cardiol.* 2020;5(7):802-810.
12. Alqahtani JS, Oyelade T, Aldhahir AM, et al. Prevalence, Severity and Mortality Associated with COPD and Smoking in Patients with COVID-19: A Rapid Systematic Review and Meta-Analysis. *PLoS One.* 2020;15(5):e0233147.
13. Chhiba KD, Patel GB, Vu THT, et al. Prevalence and characterization of asthma in hospitalized and nonhospitalized patients with COVID-19. *J Allergy Clin Immunol.* 2020;146(2):307-314.e4.
14. Drake TM, Docherty AB, Harrison EM, et al. Outcome of hospitalization for COVID-19 in patients with interstitial lung disease. *Thorax.* 2020;75(8):706-709.
15. Pagnesi M, Baldetti L, Beneduce A, et al. Pulmonary hypertension and right ventricular involvement in hospitalized patients with COVID-19. *Rev Esp Cardiol (Engl Ed).* 2020;73(10):852-858.
16. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. *Int Urol Nephrol.* 2020;52(6):1193-1194.
17. Hirsch JS, Ng JH, Ross DW, et al. Acute kidney injury in patients hospitalized with COVID-19. *Kidney Int.* 2020;98(1):209-218.
18. Jager KJ, Kramer A, Chesnaye NC, et al. Results from the ERA-EDTA Registry indicate a high mortality due to COVID-19 in dialysis patients and kidney transplant recipients across Europe. *Kidney Int.* 2020;98(6):1540-1548.
19. Akalin E, Azzi Y, Bartash R, et al. COVID-19 and Kidney Transplantation. *N Engl J Med.* 2020;382(25):2475-2477.
20. Fung M, Babik JM. COVID-19 in Immunocompromised Hosts: What We Know So Far. *Clin Infect Dis.* 2021;72(2):340-350.
21. Kuderer NM, Choueiri TK, Shah DP, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. *Lancet.* 2020;395(10241):1907-1918.
22. Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. *Lancet Oncol.* 2020;21(3):335-337.
23. Lee LYW, Cazier JB, Angelis V, et al. COVID-19 mortality in patients with cancer on chemotherapy or other anticancer treatments: a prospective cohort study. *Lancet.* 2020;395(10241):1919-1926.
24. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City. *BMJ.* 2020;369:m1966.
25. Xie J, Covassin N, Fan Z, et al. Association Between Hypoxemia and Mortality in Patients With COVID-19. *Mayo Clin Proc.* 2020;95(6):1138-1147.
26. Gidari A, De Socio GV, Sabbatini S, et al. Predictive value of National Early Warning Score 2 (NEWS2) for intensive care unit admission in patients with SARS-CoV-2 infection. *Infect Dis (Lond).* 2020;52(10):698-704.
27. Altschul DJ, Unda SR, Benton J, et al. A novel severity score to predict inpatient mortality in COVID-19 patients. *Sci Rep.* 2020;10(1):16726.
28. Carr E, Bendayan R, Bean D, et al. Evaluation and Improvement of the National Early Warning Score (NEWS2) for COVID-19: a multi-hospital study. *BMC Med.* 2021;19(1):23.
29. Herold T, Jurinovic V, Arnreich C, et al. Elevated levels of IL-6 and CRP predict the need for mechanical ventilation in COVID-19. *J Allergy Clin Immunol.* 2020;146(1):128-136.e4.
30. Fois AG, Paliogiannis P, Scano V, et al. The Systemic Inflammation Index on Admission Predicts In-Hospital Mortality in COVID-19 Patients. *Molecules.* 2020;25(23):5725.
31. Guo T, Fan Y, Chen M, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol.* 2020;5(7):811-818.
32. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol.* 2020;5(5):428-430.
33. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost.* 2020;18(4):844-847.
34. Francone M, Iafrate F, Masci GM, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. *Eur Radiol.* 2020;30(12):6808-6817.
35. Dweck MR, Bularga A, Hahn RT, et al. Global evaluation of echocardiography in patients with COVID-

10.48047/jocaaa.2024.33.06.103

19. *Eur Heart J Cardiovasc Imaging.* 2020;21(9):949-958.
36. Tobin MJ, Laghi F, Jubran A. Why COVID-19 Silent Hypoxemia is Baffling to Physicians. *Am J Respir Crit Care Med.* 2020;202(3):356-360.
37. Gattinoni L, Chiumello D, Caironi P, et al. COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Med.* 2020;46(6):1099-1102.
38. Lala A, Johnson KW, Januzzi JL, et al. Prevalence and Impact of Myocardial Injury in Patients Hospitalized With COVID-19 Infection. *J Am Coll Cardiol.* 2020;76(5):533-546.
39. Bhatla A, Mayer MM, Adusumalli S, et al. COVID-19 and Cardiac Arrhythmias. *Heart Rhythm.* 2020;17(9):1439-1444.
40. Gülcü O, Çınar T, Hayıroğlu Mİ, et al. CHA2DS2-VASc score is a predictor of in-hospital mortality in patients with COVID-19. *Thromb Haemost.* 2020;120(8):1123-1129.
41. Ruocco G, Feola M, Palazzuoli A. Prognostic role of CHA_2DS_2-VASc score in COVID-19 patients: A multicenter retrospective study. *Int J Clin Pract.* 2021;75(4):e13982.
42. Çinar T, Gülcü O, Hayıroğlu Mİ, et al. Assessment of the CHA2DS2-VASc score in predicting mortality in patients hospitalized with COVID-19 pneumonia. *Am J Emerg Med.* 2021;40:106-113.
43. Guner A, Kaya A, Kaya Y, et al. The utility of CHA_2DS_2-VASc score in predicting COVID-19 mortality. *Int J Clin Pract.* 2021;75(5):e14022.
44. Salah HM, Mehta JL. The Role of CHA_2DS_2-VASc Score in COVID-19 Prognostication: More Than a Stroke Risk Score. *J Cardiovasc Pharmacol.* 2021;78(1):e1-e3.
45. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA.* 2020;323(16):1574-1581.
46. Knight SR, Ho A, Pius R, et al. Risk stratification of patients admitted to hospital with COVID-19: validation of the 4C mortality score. *BMJ.* 2020;370:m3339.
47. Price-Haywood EG, Burton J, Fort D, Seoane L. Hospitalization and Mortality among Black Patients and White Patients with Covid-19. *N Engl J Med.* 2020;382(26):2534-2543.