ORIGINAL ARTICLE

The CHA2DS2-VASc score and in-hospital mortality in patients with COVID-19: A multicenter retrospective cohort study

COVID-19 hastalarında CHA2DS2-VASc skoru ve hastane içi mortalite: Çok merkezli geriye dönük kohort çalışması

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ABSTRACT

Objective: Coronavirus disease 2019 (COVID-19) is an infectious disease that was first reported in December 2019 in Wuhan, China, and has since spread rapidly around the world, resulting in the ongoing COVID-19 pandemic. The CHA2DS2-VASc score is a well-validated risk stratification tool for predicting stroke in atrial fibrillation (AFib), as well as morbidity and mortality in several entities. The aim of this study was to evaluate the relationship between the CHA2DS2-VASc score and in-hospital mortality in patients with COVID-19, regardless of AFib.

Methods: This multicenter, retrospective study included a total of 349 patients with COVID-19 who were hospitalized between March 15 and April 15, 2020. The CHA2DS2-VASc score of each patient was calculated. Mortality outcomes were followed up until April 25, 2020.

Results: The CHA2DS2-VASc score was significantly higher in non-survivor COVID-19 patients than in survivor COVID-19 patients (p<0.001). Forward stepwise logistic regression analysis demonstrated that a CHA2DS2-VASc score of ≥3 (odds ratio [OR]: 12.613, 95% confidence interval [CI]: 3.092–51.451; p<0.001), and the leukocyte count (OR: 1.327, 95% CI: 1.145-1.538; p<0.001), C-reactive protein level (OR: 1.010, 95% CI: 1.002–1.018; p=0.012), and ferritin level (OR: 1.005, 95% CI: 1.003–1.007; p<0.001) on admission were independent predictors of in-hospital mortality of COVID-19 patients.

Conclusion: The CHA2DS2-VASc score predicted in-hospital mortality in patients with COVID-19, regardless of AFib.

ÖZET

Amaç: Koronavirus hastalığı 2019 (COVID-19), ilk kez Aralık 2019'da Çin'in Wuhan kentinde bildirilen ve o zamandan beri dünya çapında hızla yayılan ve devam eden pandemiye neden olan bulaşıcı bir hastalıktır. CHA2DS2-VASc skoru, atriyal fibrilasyonda inmenin yanı sıra çeşitli durumlarda morbidite ve mortaliteyi tahmin etmek için iyi doğrulanmış bir risk sınıflandırma skorudur. Bu çalışmada, COVID-19 hastalarında CHA2DS2-VASc skoru ile hastane içi mortalite arasındaki ilişkiyi değerlendirmeyi amaçladık.

Yöntemler: Bu çok merkezli retrospektif çalışmaya 15 Mart ile 15 Nisan 2020 tarihleri arasında hastaneye yatırılan toplam 349 COVID-19 hastası dahil edildi. Her hastanın CHA2DS2-VASc skoru hesaplandı. Ölüm sonuçları 25 Nisan 2020'ye kadar takip edildi.

Bulgular: Hayatta kalmayan COVID-19 hastalarında CHA2DS2-VASc skorları hayatta kalanlara göre anlamlı olarak yüksekti (p<0.001). İleriye doğru aşamalı lojistik regresyon analizinde, CHA2DS2-VASc skoru ≥3 ([odds oranı] OO=12.613, %95 GA: 3.092–51.451, p<0.001), başlangıçtaki lökosit sayısı (OO=1.327, %95 GA: 1.145–1.538, p<0.001), başlangıçtaki C-reaktif protein düzeyi (OO=1.010, %95 GA: 1.002–1.018, p=0.012), ve başlangıçtaki ferritin düzeyinin (OO=1.005, %95 GA: 1.003–1.007, p<0.001) hastane içi mortalitenin bağımsız öngördürücüleri olduğu saptandı.

Sonuç: CHA2DS2-VASc skoru, atriyal fibrilasyondan bağımsız olarak COVID-19 hastalarında hastane içi mortaliteyi öngörmektedir.

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Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[1] which was first reported in December 2019 in Wuhan, Hubei province, China,[1] and has since spread rapidly around the world, resulting in the ongoing COVID-19 pandemic. SARS-CoV-2 pneumonia has been extensively studied.[2,3] Several complications of COVID-19 have been reported, including acute respiratory distress syndrome,[2] cardiac injury,[4–8] venous thromboembolism, and arterial thrombosis.[9] The overall mortality rate of the patients hospitalized due to SARS-CoV-2 pneumonia in Wuhan, China in 1 report was 4.3%.[10] However, different mortality rates have been reported worldwide.

CHA2DS2-VASc (congestive heart failure, hypertension [HT], age ≥75 years [doubled], diabetes mellitus [DM], prior stroke or transient ischemic attack [doubled], vascular disease, age 65-74 years, and sex category [female]) is a well-validated risk stratification score for predicting stroke in patients with atrial fibrillation (AFib).[11] This score has also been found to predict mortality in several conditions other than AFib.[12–15] Many individual risk factors included in this score are also risk factors for COVID-19 morbidity and mortality. The objective of this study was to assess the relationship between the CHA2DS2-VASc score and in-hospital mortality in patients with COVID-19, irrespective of AFib.

METHODS

Study population and design

The diagnosis of COVID-19 was made according to the World Health Organization's interim guidance and confirmed by RNA detection of SARS-CoV-2. The criteria for hospitalization in the hospitals where the study was conducted were consistent with those developed by the Turkish Ministry of Health, including age >50 years, moderate or severe symptoms, at least 1 risk factor on presentation (HT, DM, chronic pulmonary disease, chronic heart disease, chronic kidney failure, or immune deficiency), at least 1 poor prognostic factor (lymphopenia, high levels of C-reactive protein, ferritin, or D-dimer) and a social indication, such as inappropriate home conditions or a problem of compliance with isolation rules. Patients included in this study were diagnosed with COVID-19 and hospitalized between March 15, 2020 and April 15, 2020. The criteria for discharge were the absence of fever for at least 3 days, improvement in both lungs as observed with chest computed tomography, clinical remission of respiratory symptoms, and a throat-swab sample negative for SARS-CoV-2 RNA. The study was conducted according to the Declaration of Helsinki and was approved by an institutional ethics committee (No: 99, May 15, 2020), as well as the Ministry of Health. The need for additional written informed patient consent was waived due to the retrospective nature of the study.

Abbreviations:

AFib	*Atrial fibrillation*
CHA2DS2-VASc	*Congestive heart failure, hypertension, age ≥75 years (doubled), diabetes mellitus, prior stroke or transient ischemic attack (doubled), and vascular disease, age 65-74 years, and sex category (female)*
CI	*Confidence interval*
COVID-19	*Coronavirus disease 2019*
DM	*Diabetes mellitus*
HT	*Hypertension*
OR	*Odds ratio*
SARS-CoV-2	*Severe acute respiratory syndrome coronavirus 2*

Data collection

Epidemiological, demographic, clinical, laboratory, and mortality outcome data were obtained from patient medical records using admission numbers that were unique to each patient. Mortality outcomes were followed through April 25, 2020. The CHA2DS2-VASc score of each patient was calculated. The study population was divided into 2 groups based on in-hospital mortality: a survivor group (n=311) and a non-survivor group (n=38).

Identification of risk factors

Patients who were previously using oral antidiabetic and/or insulin therapy or those with a fasting blood glucose, measured at least twice, that was ≥126mg/dL were considered diabetic.[16] Patients who were previously on antihypertensive therapy or those with a blood pressure reading, measured at least twice, of ≥140/90 mmHg were considered hypertensive.[17] The presence of hyperlipidemia was defined by a measure of total cholesterol of >200 mg/dL or low-density lipoprotein cholesterol of >100 mg/dL or when the patient had previously used lipid-lowering medication.[18] Patients who used tobacco products at the time of admission to the hospital and those who had quit smoking within the past month were considered

smokers. Patients who had previously sustained focal neurological brain damage due to ischemia, including transient ischemic attack, were identified as patients with stroke. Patients with a reduced left ventricular ejection fraction (<40%) were identified as patients with heart failure.[19] Patients with prior myocardial infarction and those with documented obstructive atherosclerotic disease in the peripheral arteries were classified as patients with vascular disease. Both paroxysmal and chronic AFib were included as AFib.

Statistical analysis

Data analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 software (IBM Corp., Armonk, NY, USA). The normal distribution of continuous variables was assessed using the Kolmogorov-Smirnov test. Continuous variables were expressed as median (interquartile range). Categorical variables were expressed as number (percentage). The Mann-Whitney U-test was used to compare continuous variables. A chi-squared test or Fisher's exact test was used to compare categorical variables according to the fulfillment of statistical assumptions. Survival outcome according to the CHA2DS2-VASc score was compared using the Kaplan-Meier survival analysis and the log-rank test. All of the significant parameters in the univariate analysis were selected for the multivariable model and forward stepwise logistic regression analysis was used to determine the independent predictors of in-hospital mortality of COVID-19 patients. The odds ratio (OR) and 95% confidence interval (CI) of each independent variable were calculated. A 2-tailed p value of <0.05 was considered significant.

RESULTS

This multicenter, retrospective cohort study included a total of 349 hospitalized COVID-19 patients (153 male, median age: 56.0 years [range: 20.0–80.0 years]). In our study, the mortality rate was 10.8%. The CHA2DS2-VASc score was significantly higher in non-survivor COVID-19 patients than in survivor group patients (p<0.001) (Fig. 1). A comparison of baseline characteristics of the COVID-19 patients is shown in Table 1. Kaplan-Meier survival curves according to CHA2DS2-VASc scores are shown in Figure 2.

Forward stepwise logistic regression analysis was performed to determine the independent predictors of in-hospital mortality. The analysis demonstrated that a CHA2DS2-VASc score of ≥3 (OR: 12.613, 95% CI: 3.092–51.451; p<0.001), and the leukocyte count (OR: 1.327, 95% CI: 1.145–1.538; p<0.001), C-reactive protein level (OR: 1.010, 95% CI: 1.002–1.018; p=0.012), and ferritin level (OR: 1.005, 95% CI: 1.003–1.007; p<0.001) on admission were independent predictors of in-hospital mortality of COVID-19 patients (Table 2).

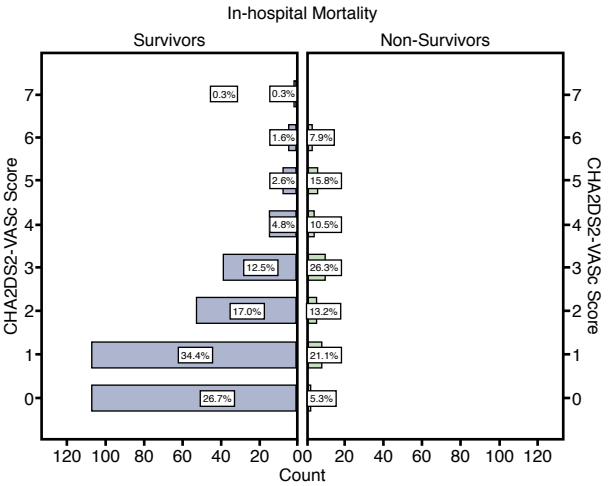

Figure 1. CHA2DS2-VASc scores in survivor and non-survivor COVID-19 patients.

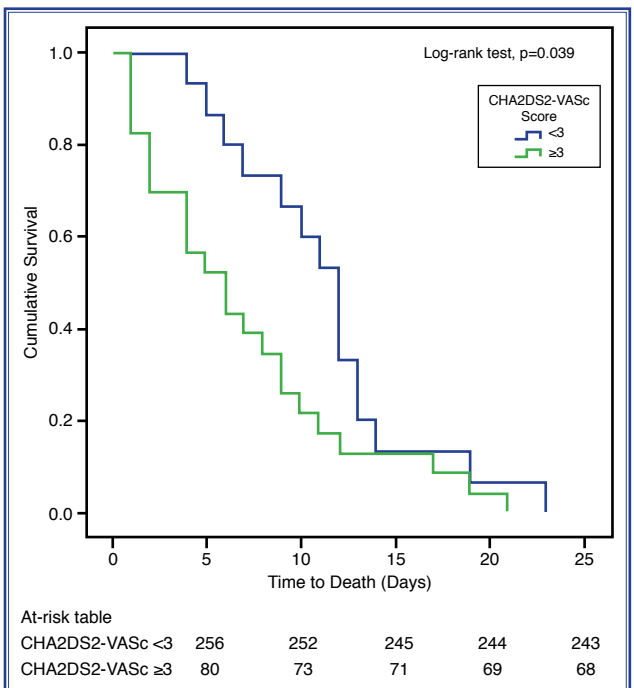

Figure 2. Kaplan–Meier survival curves according to CHA2DS2-VASc score in COVID-19 patients.

Table 1. Comparison of baseline characteristics of COVID-19 patients

Variable	Survivor (n=311)	Non-survivor (n=38)	*p* value
Gender, (male) n (%)	139 (44.7)	14 (36.8)	0.357
Body mass index (kg/m^2)	28.1 (24.7–30.0)	27.3 (24.6–31.9)	0.926
Hyperlipidemia, n (%)	33 (10.6)	12 (31.6)	0.001
Smoking, n (%)	64 (20.6)	20 (52.6)	<0.001
Chronic obstructive pulmonary disease, n (%)	18 (5.8)	9 (23.7)	**0.001**
Atrial fibrillation, n (%)	11 (3.5)	5 (13.2)	**0.021**
Hemoglobin, mmol/L	8.0 (7.0–8.8)	6.2 (5.6–7.2)	<0.001
Leukocyte count, ×10^3/uL	5.8 (4.7–7.6)	13.0 (7.5–18.4)	<0.001
Platelet count, ×10^3/uL	210.7 (167.9–282.0)	183.0 (101.3–294.3)	0.031
C-reactive protein (nmol/L)	309.5 (106.2–990.4)	1600.0 (1178.5–2228.4)	<0.001
Ferritin (nmol/L)	0.69 (0.54–0.70)	1.7 (1.39–1.80)	<0.001
CHA2DS2-VASc score			<0.001
0	83 (26.7)	2 (5.3)	
1	107 (34.4)	8 (21.1)	
2	53 (17.0)	5 (13.2)	
≥3	68 (21.9)	23 (60.4)	
CHA2DS2-VASc score components			
Heart failure, n (%)	7 (2.3)	4 (10.5)	0.023
Hypertension, n (%)	101 (32.5)	20 (52.6)	0.014
Age (years)	55.0 (41.0–61.0)	69.0 (60.0–76.0)	<0.001
Age <65, n (%)	266 (85.5)	15 (39.5)	–
Age 65–74, n (%)	36 (11.6)	10 (26.3)	–
Age ≥75, n (%)	9 (2.9)	13 (34.2)	–
Diabetes mellitus, n (%)	93 (29.9)	13 (34.2)	0.586
Stroke, n (%)	5 (1.6)	2 (5.3)	0.171
Vascular disease, n (%)			
Coronary artery disease	29 (9.3)	14 (36.8)	<0.001
Peripheral artery disease	9 (2.9)	2 (5.3)	0.341
Sex (female), n (%)	172 (55.3)	24 (63.2)	0.357
Treatments, n (%)			
Antibiotics	283 (91.0)	36 (94.7)	0.921
Antiviral treatment	302 (97.1)	38 (100.0)	0.973
Hydroxychloroquine	311 (100.0)	38 (100.0)	–
Mechanical ventilation, n (%)	60 (19.3)	38 (100.0)	<0.001
Admission to intensive care unit, n (%)	58 (18.6)	30 (78.9)	<0.001
Cause of death, n (%)			
Acute kidney injury	–	4 (10.5)	–
Acute respiratory distress syndrome	–	7 (18.4)	–
Multiple organ failure	–	24 (63.2)	–
Sepsis	–	3 (7.9)	–

Data are presented as number (%) or median (interquartile range). P value was calculated using an independent samples t-test or the Mann-Whitney U-test for continuous variables and a chi-squared test or the Fisher's exact test for categorical variables, as appropriate. A p value <0.05 was considered significant.

Table 2. Univariate and multivariate analysis of in-hospital mortality

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	p value	OR (95% CI)	*p* value
Hyperlipidemia, n (%)	3.888 (1.794–8.426)	0.001	–	–
Smoker, n (%)	4.288 (2.143–8.580)	<0.001	–	–
COPD, n (%)	5.052 (2.082–12.258)	<0.001	–	–
AFib, n (%)	4.132 (1.353–12.621)	0.013	–	–
CHA2DS2-VASc score ≥3	5.479 (2.711–11.077)	<0.001	12.613 (3.092–51.451)	**<0.001**
Hemoglobin, mmol/L	0.531 (0.429–0.657)	<0.001	–	–
Leukocyte count, $\times 10^3$/uL	1.335 (1.227–1.452)	<0.001	1.327 (1.145–1.538)	**<0.001**
Platelet count, $\times 10^3$/uL	0.996 (0.992–1.000)	0.066	–	–
C-reactive protein (nmol/L)	1.012 (1.008–1.017)	<0.001	1.010 (1.002–1.018)	**0.012**
Ferritin (nmol/L)	1.005 (1.003–1.007)	<0.001	1.005 (1.003–1.007)	**<0.001**

A p value <0.05 was considered significant. AFib: Atrial fibrillation; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; OR: Odds ratio.

DISCUSSION

The major finding of our study is that the CHA2DS2-VASc score predicted in-hospital mortality in patients with COVID-19 regardless of the presence of AFib. The CHA2DS2-VASc score is a well-validated risk stratification score for estimating the risk of ischemic stroke, thromboembolism, and mortality in patients with non-valvular AFib.[20] This score clusters multiple cardiovascular risk factors and its usefulness has also been proposed in several other entities.[21,22] To the best of our knowledge, this is the first report in the literature to evaluate the relationship between the CHA2DS2-VASc score and in-hospital mortality in COVID-19 patients.

Several studies have reported a substantial association between pneumonia and in-hospital cardiovascular events, including acute coronary syndrome, heart failure, AFib, and mortality.[23–27] Assessing the CHA2DS2-VASc score in hospitalized COVID-19 patients can help identify patients at high risk of death, such as those with a CHA2DS2-VASc score of ≥3. This warrants rhythm monitoring to detect pre-arrhythmic states, initiating early treatment with anti-arrhythmic and anticoagulant agents,[20] and caution regarding the use of drugs with higher arrhythmogenic and cardiac event potential, such as fluoroquinolones and macrolides.[28–31]

Many individual risk factors included in the CHA2DS2-VASc score are risk factors associated with COVID-19 morbidity and mortality. Chen et al.[3] evaluated 99 patients with COVID-19 and reported that 40% of the patients had underlying cardiovascular or cerebrovascular disease. Also, Huang et al.[2] assessed 41 patients with COVID-19 and demonstrated that 32% of the patients had underlying diseases, including cardiovascular disease (15%), HT (15%), and DM (20%). Wang et al.[10] investigated a total of 138 hospitalized patients with COVID-19 and revealed that 46.4% had 1 or more comorbidities, including HT (31%), DM (10%), and cardiovascular disease (14.5%). Yang et al.[32] reported that the rate of coexisting comorbidities and 28-day mortality among 52 critically ill COVID-19 patients who were admitted to the intensive care unit was 40% and 61.5%, respectively. The incidence of cardiovascular and cerebrovascular disease in survivors vs. non-survivors was 20% vs. 53% and 0% vs. 22%, respectively. Also, Zhou et al.[33] reported that the mortality rate among 191 COVID-19 patients was 28.3%. Fatal cases had a higher rate of comorbidities, including HT (48% vs. 23%), DM (31% vs.14%), coronary artery disease (24% vs. 1%), acute cardiac injury (59% vs 1%), and heart failure (52% vs 12%) when compared with survivors.[33] Zhang et al.[34] have recently reported that older patients and those with chronic disease were more likely to exhibit severe forms of COVID-19, show no improvement, and have a higher in-hospital mortality rate. Moreover, the presence of respiratory, cardiovascular, and endocrine system diseases was associated with disease severity. Similarly, cardiovas-

cular diseases, endocrine system disease, and respiratory system disease were the 3 most common coexisting chronic diseases in this study.

In our study, the mortality rate was 10.8%. This rate was higher than that reported in some other studies.[10,34] This heterogeneity is probably due to differences in the illness severity of the patients. Among our patients, 25.2% were critically ill and admitted to the intensive care unit. The incidence of hyperlipidemia, HT, coronary artery disease, heart failure, chronic obstructive pulmonary disease, and AFib was significantly higher in non-survivors than in survivors ($p<0.05$). The CHA2DS2-VASc scores were significantly higher in non-survivor COVID-19 patients than in survivor COVID-19 patients.

It has been demonstrated that increased leukocyte, C-reactive protein, and ferritin levels on hospital admission were significantly associated with critical disease conditions, as well as with higher in-hospital mortality.[34,35] In our study, elevated leukocyte count, C-reactive protein, and ferritin levels on admission were independently associated with in-hospital mortality in COVID-19 patients.

As yet, there is a lack of well-validated scoring systems for risk prediction in COVID-19. The CHA2DS2-VASc scoring system is a simple yet effective tool for fast risk stratification in different entities.[12–15] Our study results indicated that, rather than individual factors of the CHA2DS2-VASc score, the total score demonstrated a prognostic performance for mortality in COVID-19 patients. This score may serve as a simplified means of rapid risk assessment on hospital admission, which could contribute to determining high-risk patients and guiding early treatment and close follow-up, including advising the family.

Limitations

Our study has several limitations. First, it should be noted that our results are based on a retrospective study with a relatively small number of patients. Therefore, larger prospective studies are required to validate the significance of the relationship between the CHA2DS2-VASc score and mortality in patients with COVID-19. Second, the vascular disease component of the score denotes the presence of prior myocardial infarction, peripheral artery disease, or aortic plaque. Due to the retrospective design of our study, information about aortic plaque was not necessarily available from the patient files. Third, we did not include information regarding medications used by the patients, including angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. Finally, we have only reported in-hospital mortality, as a consequence of the retrospective design. Further survival studies are warranted for data regarding short- and long-term outcomes.

Conclusion

Non-survivor COVID-19 patients had higher CHA2DS2-VASc scores than survivors. Also, a CHA2DS2-VASc score of ≥3 on hospital admission predicted in-hospital mortality of COVID-19 patients. Assessing the CHA2DS2-VASc score on hospital admission may contribute to risk stratification in the COVID-19 pandemic.

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REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020;382:727–33. [CrossRef]
2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497–506. [CrossRef]
3. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507–13. [CrossRef]
4. Hendren NS, Drazner MH, Bozkurt B, Cooper LT Jr. Description and Proposed Management of the Acute COVID-19 Cardiovascular Syndrome. Circulation 2020;141:1903–14.
5. Deng Q, Hu B, Zhang Y, Wang H, Zhou X, Hu W, et al. Suspected myocardial injury in patients with COVID-19: Evidence from front-line clinical observation in Wuhan, China. Int J Cardiol 2020;311:116–21. [CrossRef]
6. Ammirati E, Wang DW. SARS-CoV-2 inflames the heart. The importance of awareness of myocardial injury in COVID-19

patients. Int J Cardiol 2020;311:122–3. [CrossRef]
7. Kochi AN, Tagliari AP, Forleo GB, Fassini GM, Tondo C. Cardiac and arrhythmic complications in patients with COVID-19. J Cardiovasc Electrophysiol 2020;31:1003–8.
8. Mishra AK, Sahu KK, Lal A, Sargent J. Patterns of heart injury in COVID-19 and relation to outcome. J Med Virol. 2020 Apr 8. doi: 10.1002/jmv.25847. [Epub ahead of print]. [CrossRef]
9. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020;191:145–7. [CrossRef]
10. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020;323:1061–9. [CrossRef]
11. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 2010;137:263–72. [CrossRef]
12. Saliba W, Gronich N, Barnett-Griness O, Rennert G. Usefulness of CHADS2 and CHA2DS2-VASc Scores in the Prediction of New-Onset Atrial Fibrillation: A Population-Based Study. Am J Med 2016;129:843–9. [CrossRef]
13. Huang FY, Huang BT, Pu XB, Yang Y, Chen SJ, Xia TL, et al. CHADS2, CHA2DS2-VASc and R2CHADS2 scores predict mortality in patients with coronary artery disease. Intern Emerg Med 2017;12:479–86. [CrossRef]
14. Hong C, Alluri K, Shariff N, Khattak F, Adelstein E, Jain S, et al. Usefulness of the CHA2DS2-VASc Score to Predict Mortality in Defibrillator Recipients. Am J Cardiol 2017;120:83–6. [CrossRef]
15. Koeda Y, Komatsu T, Matsuura Y, Morioka H, Uchimura Y, Taguchi Y, et al. CHADS2 and modified CHA2DS2-VASc scores for the prediction of congestive heart failure in patients with nonvalvular atrial fibrillation. J Arrhythm 2017;33:488–93. [CrossRef]
16. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 2003;26:S5–20. [CrossRef]
17. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al; ESC Scientific Document Group. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021–104. [CrossRef]
18. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002;106:3143–421. [CrossRef]
19. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;37:2129–200.
20. Kirchhof P, Benussi S, Kotecha D, Ahlsson A, Atar D, Casadei B, et al. 2016 ESC Guidelines for the Management of Atrial Fibrillation Developed in Collaboration With EACTS. Rev Esp Cardiol (Engl Ed) 2017;70:50. [CrossRef]
21. Melgaard L, Gorst-Rasmussen A, Lane DA, Rasmussen LH, Larsen TB, Lip GY. Assessment of the CHA2DS2-VASc Score in Predicting Ischemic Stroke, Thromboembolism, and Death in Patients With Heart Failure With and Without Atrial Fibrillation. JAMA 2015;314:1030–8. [CrossRef]
22. Chen YL, Cheng CL, Huang JL, Yang NI, Chang HC, Chang KC, et al; TSOC-HFrEF Registry investigators and committee. Mortality prediction using CHADS2/CHA2DS2-VASc/R2CHADS2 scores in systolic heart failure patients with or without atrial fibrillation. Medicine (Baltimore) 2017;96:e8338. [CrossRef]
23. Corrales-Medina VF, Musher DM, Shachkina S, Chirinos JA. Acute pneumonia and the cardiovascular system. Lancet. 2013;381:496–505. [CrossRef]
24. Corrales-Medina VF, Musher DM, Wells GA, Chirinos JA, Chen L, Fine MJ. Cardiac complications in patients with community-acquired pneumonia: incidence, timing, risk factors, and association with short-term mortality. Circulation 2012;125:773–81. [CrossRef]
25. Violi F, Cangemi R, Falcone M, Taliani G, Pieralli F, Vannucchi V, et al; SIXTUS (Thrombosis-Related Extrapulmonary Outcomes in Pneumonia) Study Group. Cardiovascular Complications and Short-term Mortality Risk in Community-Acquired Pneumonia. Clin Infect Dis 2017;64:1486–93. [CrossRef]
26. Mandal P, Chalmers JD, Choudhury G, Akram AR, Hill AT. Vascular complications are associated with poor outcome in community-acquired pneumonia. QJM 2011;104:489–95.
27. Cangemi R, Calvieri C, Falcone M, Bucci T, Bertazzoni G, Scarpellini MG, et al; SIXTUS Study Group. Relation of Cardiac Complications in the Early Phase of Community-Acquired Pneumonia to Long-Term Mortality and Cardiovascular Events. Am J Cardiol 2015;116:647–51.
28. van der Hooft CS, Heeringa J, van Herpen G, Kors JA, Kingma JH, Stricker BH. Drug-induced atrial fibrillation. J Am Coll Cardiol 2004;44:2117–24. [CrossRef]
29. Postma DF, Spitoni C, van Werkhoven CH, van Elden LJR, Oosterheert JJ, Bonten MJM. Cardiac events after macrolides or fluoroquinolones in patients hospitalized for community-acquired pneumonia: post-hoc analysis of a cluster-randomized trial. BMC Infect Dis 2019;19:17. [CrossRef]
30. Rao GA, Mann JR, Shoaibi A, Bennett CL, Nahhas G, Sutton SS, et al. Azithromycin and levofloxacin use and in-

creased risk of cardiac arrhythmia and death. Ann Fam Med 2014;12:121–7. [CrossRef]

31. Trifirò G, de Ridder M, Sultana J, Oteri A, Rijnbeek P, Pecchioli S, et al. Use of azithromycin and risk of ventricular arrhythmia. CMAJ 2017;189:E560-E8. [CrossRef]
32. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020;8:475–81.
33. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054–62. [CrossRef]
34. Zhang J, Wang X, Jia X, Li J, Hu K, Chen G, et al. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. Clin Microbiol Infect 2020;26:767–72. [CrossRef]
35. Huang I, Pranata R, Lim MA, Oehadian A, Alisjahbana B. C-reactive protein, procalcitonin, D-dimer, and ferritin in severe coronavirus disease-2019: a meta-analysis. Ther Adv Respir Dis 2020;14:1753466620937175. [CrossRef]

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