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The HEARRT-C Score: Is Aspirin Protective in COVID-19 Patients? A Single-Centre Retrospective Study

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Abstract: This study aimed to develop a scoring system to predict mortality risk in hospitalised COVID-19 patients using clinical, laboratory, and imaging data. A retrospective analysis was conducted at a single centre, including 325 patients admitted between March 2020 and December 2021. The data collected included patient demographics, laboratory results, medications, and thoracic CT images. Pulmonary involvement was assessed using the CO-RADS classification, while coronary artery calcification (CAC), aortic calcification, and epicardial adipose tissue were evaluated with specific scoring methods. Mortality predictors were identified through univariate and multivariate Cox proportional hazards models. The key mortality predictors identified in this study were an age above 67 years, elevated high-sensitivity troponin levels, a heart rate greater than 100 bpm, an oxygen saturation below 90%, the presence of CAC and aortic calcification, low haemoglobin levels, and the absence of acetylsalicylic acid (ASA) use at admission. The developed HEARRT-C scoring system demonstrated a strong predictive ability, with an area under the curve (AUC) of 0.91, showing 81% sensitivity and 86% specificity for predicting mortality. This study concluded that the HEARRT-C score is an effective tool for early risk stratification in COVID-19 patients, which may guide management decisions and emphasise the importance of cardiovascular factors and the potential protective role of ASA.

Keywords: COVID-19; coronary artery calcium; aortic calcifications; thorax CT; acetylsalicylic acid; primary prevention; viral infections

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1. Introduction

Since 2019, the Coronavirus Disease 2019 (COVID-19) outbreak has led to 7 million fatalities worldwide and active COVID-19 cases, and the long-term effects of COVID-19 continue to endure [1]. It has been shown that COVID-19 patients with cardiovascular diseases experience increased rates of mortality and morbidity [2].

Pulmonary findings from thoracic computed tomography (CT) scans are regularly utilised in diagnostic processes, risk classification, and disease management. Besides pulmonary findings, thoracic CT allows for the visualisation of calcium in the coronary arteries (CAC) and calcification in the thoracic aorta and epicardial adipose tissue (EAT). The presence and the degree of CAC, the presence of calcification in the aorta, and the EAT thickness were demonstrated to be linked with a poorer prognosis in COVID-19

patients [3–5]. Additionally, it has been shown that high-sensitivity troponin (hs-T) is elevated by multiple mechanisms in these patients, and elevated hs-T is associated with mortality [6].

The World Health Organization (WHO)'s COVID-19 epidemiological update revealed a general rise in new hospitalisations and a recent increase in new Intensive Care Unit (ICU) admissions [7]. Therefore, prediction tools are still needed to determine patients with a higher mortality risk to enhance patient outcomes.

The disease can lead to a variety of cardiovascular complications, including acute coronary syndrome (ACS), heart failure (HF), stroke, myocarditis, arrhythmia, and cardiac arrest. Existing scoring systems for predicting mortality in hospitalised patients, such as SIRS, NEWS, MEWS, 4C Mortality, and qSOFA, were primarily developed to assess sepsis and septic shock [8]. While some models have been specifically tailored for COVID-19, our study uniquely integrates cardiac biomarkers and coronary/aortic calcification—two key factors significantly contributing to mortality [9,10].

This work aims to design a scoring model based on the clinical, laboratory, and radiographic findings at admission in a patient population hospitalised due to COVID-19 and to enable the early identification of high-risk patients.

2. Materials and Methods

2.1. Patients

Between March 2020 and December 2021, a total of 1068 consecutive patients who tested positive for COVID-19 through the polymerase chain reaction (PCR) at our hospital were retrospectively screened. Among these, 325 hospitalised patients were enrolled in this study. The inclusion criteria required the patients to be aged 18 years or older with a confirmed COVID-19 diagnosis and have available clinical, laboratory, and imaging data. The exclusion criteria included patients with less than one year of life, those with negative COVID-19 PCR tests, those without thoracic CT imaging, or those with incomplete data.

Hospitalised COVID-19 patients were screened between 1 March 2020 and 31 December 2021. Outpatients (n = 531) were excluded due to the inability to monitor hs-troponin levels and other laboratory parameters. Patients whose initial imaging was performed using chest X-ray rather than thoracic CT (n = 159) were also excluded, as calcification scoring could not be performed. Additionally, 53 hospitalised patients with incomplete data were excluded from this study.

The statistical justification for sample size calculation is elaborated upon below. Using G*Power 3.1.9.7 software, the required sample size was determined based on a dependent two-sample *t*-test, with a power of 95%, an α error probability of 0.05, and a medium effect size (Cohen's d = 0.5). While the minimum required sample size was 95 patients, we included 325 patients in this study, utilising their most recent thoracic CT scans for analysis.

The demographic information of the patients, laboratory data at the time of hospital admission, electrocardiogram (ECG) results, medications used, in-hospital mortality, and morbidities were recorded from the institutional medical recording system. Subjects with a Blood Pressure (BP) of $\geq$140/90 mmHg (Stage 2 or greater) at presentation or those on regular antihypertensive medication were classified as having hypertension (HT). Patients exhibiting fasting blood glucose values of $\geq$126 mg/dL or HbA1c levels of $\geq$6.5% at presentation, or those on regular antidiabetic medication, were classified as having diabetes mellitus (DM). Patients with a glomerular filtration rate (GFR) of $\leq$60 mL/min/1.73 m^2 (Stage 3 or above) according to the Kidney Disease: Improving Global Outcomes (KDIGO) classification were considered to have chronic kidney disease (CKD). Patients with an FEV1/FVC ratio of $\leq$70% on pulmonary function testing or those on regular bronchodilator therapy were assigned as having chronic obstructive pulmonary disease (COPD). Patients

with a total cholesterol (TC) level of ≥240 mg/dL, low-density lipoprotein (LDL) level of ≥160 mg/dL, or triglyceride (TG) level of ≥200 mg/dL, or those on regular lipid-lowering therapy, were classified as having hyperlipidaemia (HL). Subjects with a record of ischaemic or haemorrhagic stroke were evaluated as having experienced a cerebrovascular event (CVE). Finally, patients with a history of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), or those found to have ≥50% stenosis in any coronary artery on invasive or non-invasive imaging, were classified as having coronary artery disease (CAD).

Approval for this study was obtained from our institutional ethics committee (2022/26-04, 17 August 2022). In our study, we utilised artificial intelligence for language editing. Informed consent was obtained from the patients included in this study both verbally and in writing.

Thoracic CT images were taken during hospital admission and classified according to the CO-RADS classification regarding COVID-19 involvement. CO-RADS 1–3 was considered negative involvement (mild), and 4–5 was regarded as positive involvement (moderate–severe) (Figure 1) [11]. Subsequently, visual CAC was calculated using the Weston scoring method, which correlates with the Agatston score [12]. Each of the right coronary artery (RCA), left main coronary artery (LMCA), left anterior descending artery (LAD), and left circumflex artery (LCx) was assigned a grading of 0 to 3 for the existence and degree of calcium: 0 (none), 1 (less than one-third of the artery length calcified), 2 (less than two-thirds calcified or a score between 1 and 3), and 3 (two-thirds or more calcified). The scores from the four arteries were aggregated to produce a potential score range of 0 to 12. Based on the total score range, the classification was further categorised as no calcification (0), mild (1–4), moderate (5–8), and severe (Figure 2) [12]. For the ease of use of the scoring system, CAC was also grouped as present/absent (Figure 3).

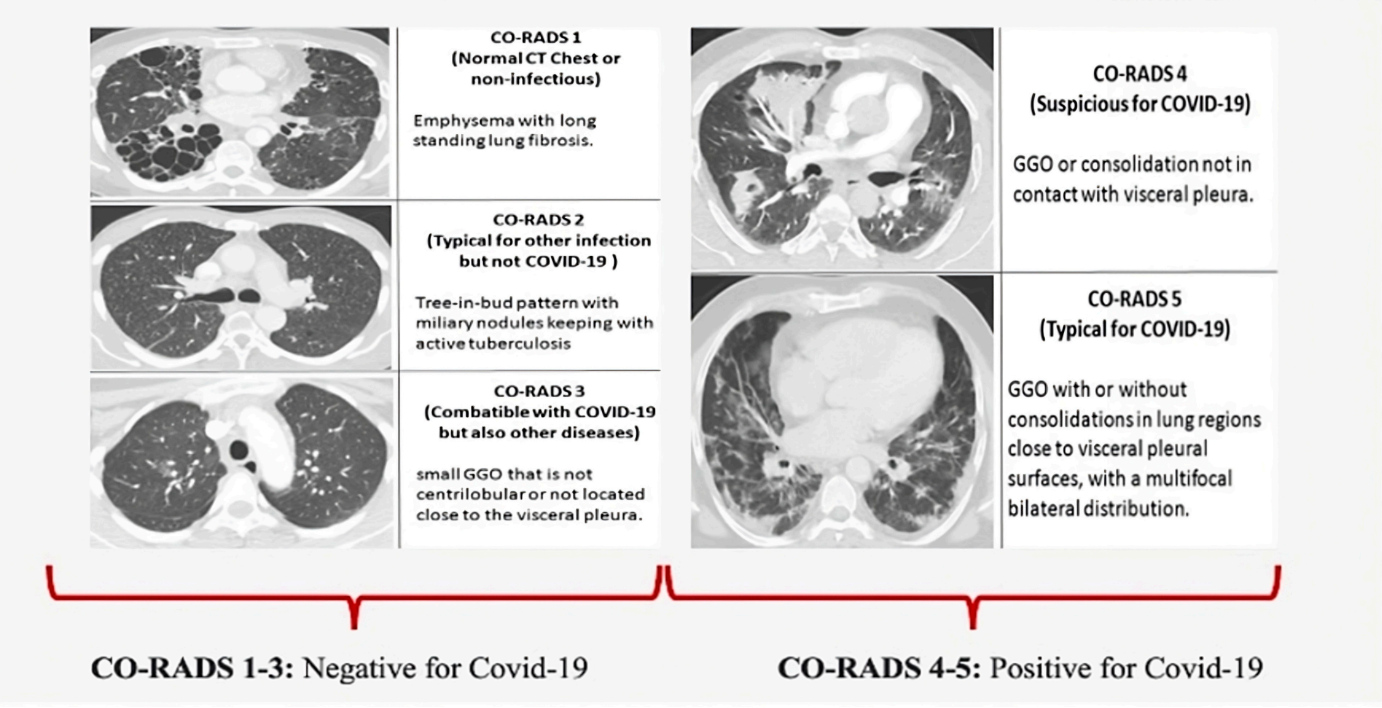


Figure 1. CO-RADS classification of COVID-19 involvement and scoring on the HEARTT-C score. CO-RADS 1–3: negative involvement for COVID-19 in scoring. CO-RADS 4–5: positive involvement for COVID-19 in scoring.

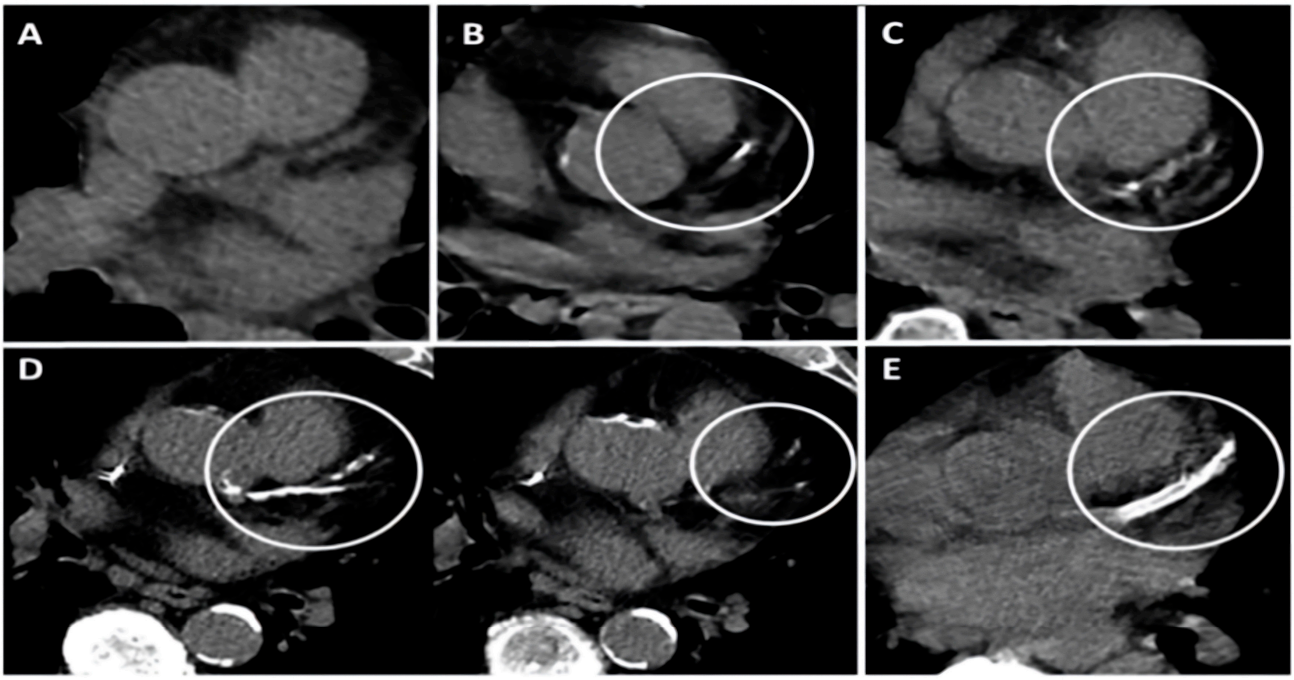


Figure 2. Visual coronary calcium score calculation with Weston score. Visual CAC calculation for LAD (area inside the white ring). (**A**): CAC:0; (**B**): CAC:1; (**C**): CAC:2; (**D**): CAC:3; (**E**): coronary stent view.

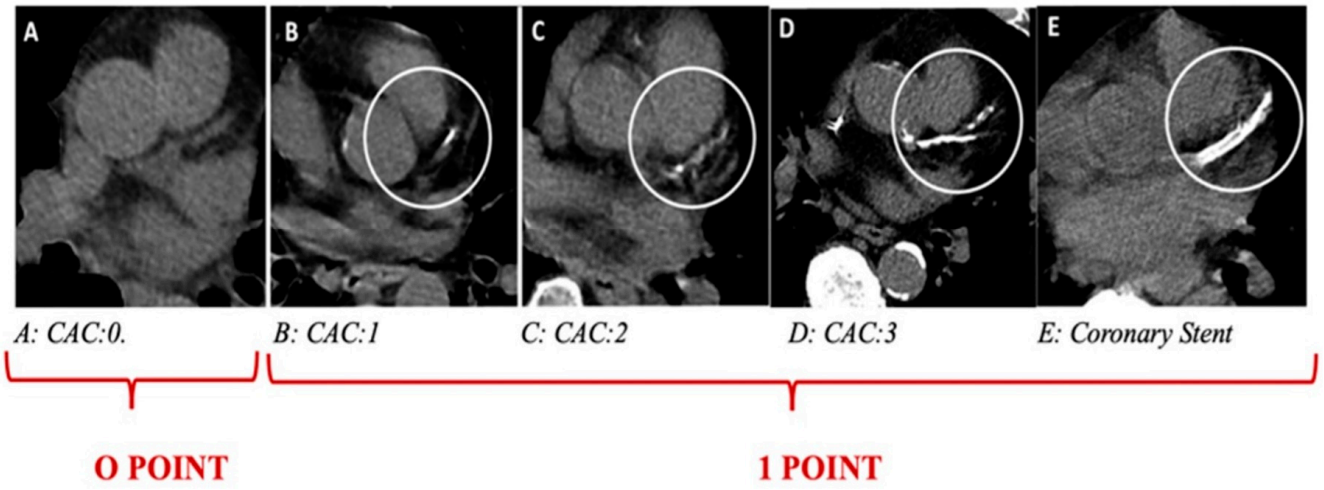


Figure 3. CAC from HEARRT-C score parameters as present/absent (+/−) on thorax CT. (**A**): CAC:0 (absent)—corresponds to 0 points in the score. (**B**–**E**): CAC > 0 (present)—corresponds to 1 point in the score.

The radiology imaging system 'SECTRA IDS7' software was used for aortic calcification to identify bright areas with a density of 130 Hounsfield Units (HU) and a minimum volume of 0.5 mm^3 as calcification. Aortic calcification was considered present if there was a brightly visible aortic plaque from the ascending aorta to the diaphragm (Figure 4). Aortic valve calcifications and abdominal aorta measurements were not included.

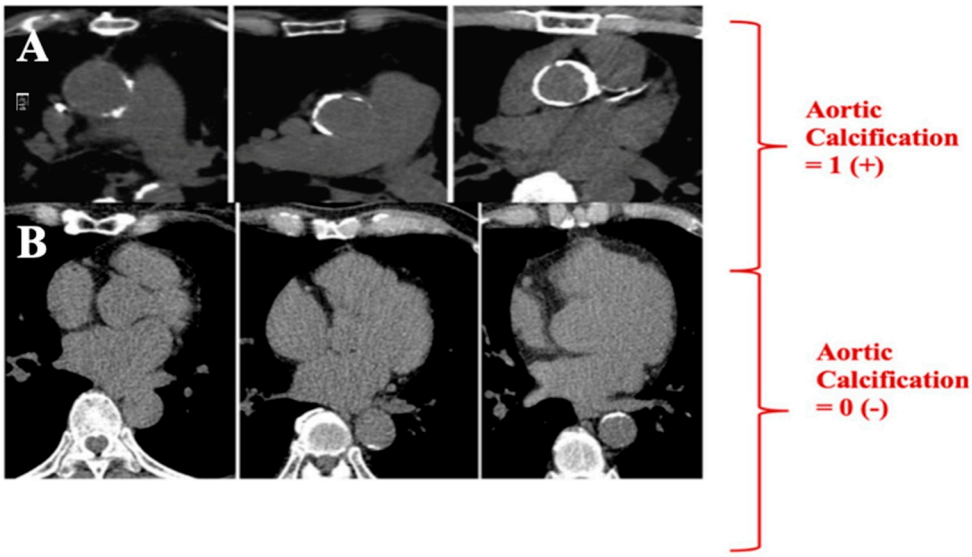


Figure 4. Aortic calcification from HEARRT-C score parameters as present/absent (+/−) on thorax CT. (**A**): aortic calcification: 1 (present)—corresponds to 2 points in the score. (**B**): aortic calcification: 0 (absent)—corresponds to 0 points in the score.

EAT was considered for all tissues within the parietal pericardium with densities between −190 and −30 HU. The average of measurements taken in a 1 cm^2 area in the right atrioventricular groove (AVO) and anterior AVO regions was calculated (Figure 5) [5]. All radiological evaluations were performed under the supervision of radiology specialists.

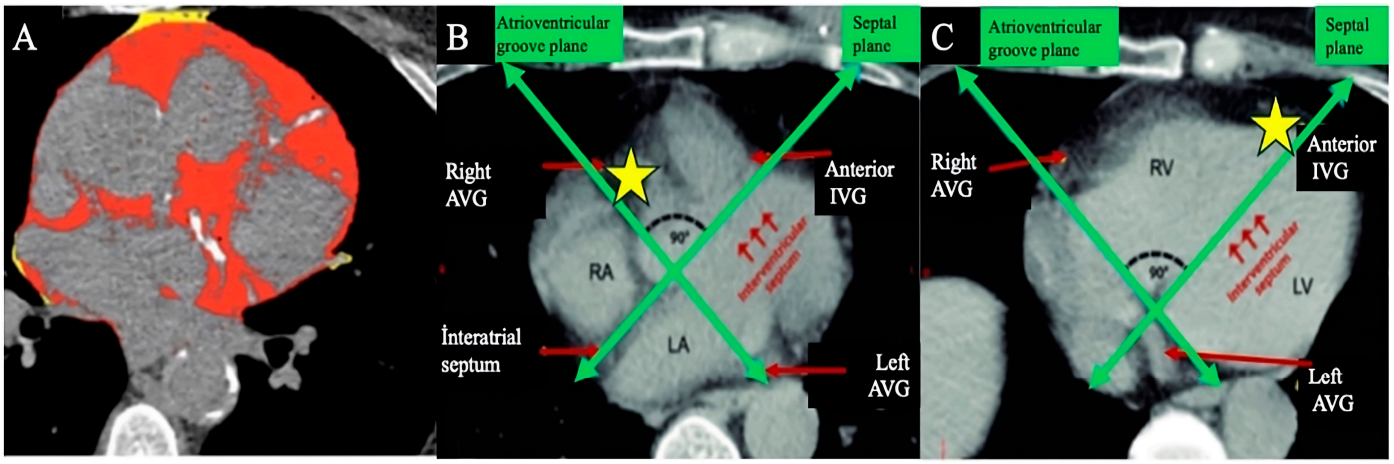


Figure 5. Epicardial adipose tissue—thorax CT. EFT measurement: average of the measurements made in the right atrioventricular groove (yellow star) and anterior atrioventricular groove (yellow star) in a 1 cm^2 area (values between −190 HU and −30 HU).

2.2. Data Analysis

Data analysis was conducted with SPSS version 26 (SPSS Inc., Chicago, IL, USA). The normality of continuous variables was verified using histograms and the Kolmogorov–Smirnov test. Continuous data are presented as the median (interquartile range) and mean ± standard deviation. As appropriate, group differences were assessed using the Chi-square test, Mann–Whitney U test, and Student's t-test. Variables with a significance level of $p < 0.1$ from these tests were incorporated into univariate Cox proportional hazards models. Hazard ratios (HRs) and 95% confidence intervals (CIs) were computed from univariate and multivariate Cox models. Clinically significant variables identified in the univariate

analysis were included in the multivariate analysis. Prior to this, multicollinearity was checked to prevent the inclusion of highly correlated or redundant variables.

The power of the HEARRT-C score to predict in-hospital mortality was examined through receiver operating characteristic (ROC) curve analysis, and area under the curve (AUC) values were determined. A threshold of $p < 0.05$ was applied to establish statistical significance.

In developing the HEARRT-C scoring system, commonly used scoring systems in clinical cardiology, such as CHA2DS2VASc, HASBLED, and H2FPEF, were used as models. The ROC curve analysis determined 10–12 predictive values for numerical variables [13–15]. All prognostic predictors identified by multivariate logistic regression analysis were scored according to their 'Odds Ratio' (OR) values. The HEARRT-C scoring system was created, and HEARRT-C scores were calculated for all patients. The threshold value for the HEARRT-C score was determined using ROC analysis.

3. Results

The patients' initial demographic and clinical characteristics are detailed in Table 1. The mean age of the subject cohort was 63 ± 16 years, and 41.5% (n = 135) of the patients were female. HT was present in 59.1% (n = 192), DM was observed in 31.1% (n = 101), and CAD was found in 13.2% (n = 43) of the subjects. Forty-five (13.8%) of the patients had active malignancy. Fifty-six (17.2%) of the patients were using acetylsalicylic acid (ASA), thirty-one (9.5%) of the patients were using angiotensin-converting enzyme inhibitors (ACEIs), and twenty-five (7.7%) of the patients were using angiotensin receptor blockers (ARBs).

Table 1. Demographical and clinical data of patients.

Demographical and Clinical Data	
Age, years	63 ± 16
BMI, kg/m^2	32.2 ± 11.3
Sex, female, n (%)	135 (%41.5)
HT, n (%)	192 (%59.1)
DM, n (%)	101 (%31.1)
CKD, n (%)	66 (%20.3)
COPD, n (%)	44 (%13.5)
HL, n (%)	51 (%15.7)
Malignancy, n (%)	45 (%13.8)
CVE, n (%)	35 (%10.7)
Smoking, n (%)	148 (%45.5)
CAD, n (%)	43 (%13.2)
ECG, SR, n (%)	277 (%85.2)
Heart rate > 100 bpm, n (%)	86 (%26.5)
ASA users, n (%)	56 (%17.2)
P2Y12 inhibitor users, n (%)	22 (%6.8)
OAC users, n (%)	22 (%6.8)
LMWH users, n (%)	42 (%12.9)
ACEI users, n (%)	31 (%9.5)
ARB users, n (%)	25 (%7.7)
BB users, n (%)	58 (%17.8)
CCB users, n (%)	29 (%8.9)
Statin users, n (%)	45 (%13.8)
Anti-anginal users, n (%)	8 (%2.5)
MRA users, n (%)	10 (%3)
Loop diuretic users, n (%)	34 (%10.5)
SGLT-2 inhibitor users, n (%)	12 (%3.7)

Abbreviations: ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ASA: acetylsalicylic acid; BB: beta-blocker; BMI: body mass index; CAD: coronary artery disease; CCB: calcium-channel blocker; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CVE: cerebrovascular event; ECG: electrocardiogram; HL: hyperlipidaemia; MRA: Mineralocorticoid Receptor Antagonist; OAC: oral anticoagulant; SR: sinus rhythm.

The mean follow-up duration was 12.9 ± 8.9 months, and 104 (32%) patients died during this period. In-hospital mortality occurred in 67 (64%) of the patients. Of these deaths, 6.7% occurred by day 10, 20% by the first month, and 25% by the third month.

Data comparing the demographic, clinical, ECG, and laboratory factors between deceased and surviving patients are presented in Table 2. Compared to survivors, deceased patients were older [70.9 ± 12.2 vs. 57.5 ± 14.3, (p = 0.005)] and had a lower body mass index (BMI) [24.5 ± 12.0 vs. 32.7 ± 11.1 (p = 0.027)]. Among the clinical data, the presence of HT (p = 0.011), CKD (p < 0.001), malignancy (p < 0.001), CVE (p = 0.048), and CAD (p = 0.029) was markedly higher in deceased patients. ECG findings revealed that the presence of sinus rhythm (SR) and HR > 100 bpm was substantially higher in deceased patients (p = 0.001 and p < 0.001, respectively). Among medications, the usage of ASA (p < 0.001), LMWH (p = 0.022), ACEI (p = 0.001), ARB (p < 0.001), beta-blockers (BB) (p < 0.001), and calcium-channel blockers (CCBs) (p = 0.009) was more common in surviving patients. Among the laboratory data, the haemoglobin (Hb) (p < 0.001), TC (p = 0.001), high-density lipoprotein (HDL) (p < 0.001), and LDL cholesterol (p = 0.004) levels were notably lower in deceased subjects. However, the white blood count (WBC) (p < 0.001), lymphocyte (p < 0.001), creatinine (p < 0.001), AST (p = 0.003), LDH (p < 0.001), and ferritin (p < 0.001) levels were significantly higher in deceased patients. Similarly, the hs-T (p < 0.001) and saturation (p < 0.001) levels at presentation were also lower in deceased patients. As expected, ICU hospitalisation was more prevalent in deceased patients (p < 0.001).

Table 2. Comparison of demographic, clinical, and laboratory data between dead and surviving patients.

	Dead n: 104	**Survived n: 221**	***p* Value**
Age, years	70.9 ± 12.2	57.5 ± 14.3	0.005
BMI, kg/m^2	24.5 ± 12.0	32.7 ± 11.1	0.027
Sex, female, n (%)	39 (37.5)	96 (44.4)	0.31
HT, n (%)	72 (69)	120 (55)	0.011
DM, n (%)	35 (34)	66 (30)	0.49
CKD, n (%)	39 (37.5)	27 (12)	<0.001
COPD, n (%)	16 (15.4)	28(12.6)	0.50
HL, n (%)	15(14.4)	36 (16)	0.66
Smoking, n (%)	52 (50)	96 (43.4)	0.26
Malignancy, n (%)	29 (27.8)	16 (7.2)	<0.001
CVE, n (%)	17 (16.3)	18 (8)	0.048
CAD, n (%)	20 (19)	23(10.4)	0.029
ECG, non-SR, n (%)	26 (25)	23(10.4)	0.001
Heart Rate > 100 bpm, n (%)	49 (47)	37(16.7)	<0.001
Saturation, %	89 (85–92)	94 (92–96)	<0.001
ICU need, n (%)	72 (69)	12 (5.4)	<0.001
ASA users, n (%)	4 (3.8)	52 (23.5)	<0.001
P2Y12 inhibitor users, n (%)	3 (2.8)	19(8.5)	0.056
OAC users, n (%)	4(3.8)	18(8)	0.150
LMWH users, n (%)	7(6.7)	35 (15.8)	0.022
ACE-I users, n (%)	2(1.9)	29 (13)	0.001
ARB users, n (%)	0 (0)	25(11.3)	<0.001
BB users, n (%)	7 (6.7)	51 (23)	<0.001
CCB users, n (%)	3(2.8)	26 (12)	0.009
Statin users, n (%)	4(3.8)	41 (18.5)	<0.001
Anti-anginal users, n (%)	1(0.96)	7 (0.03)	0.231
MRA users, n (%)	1(0.96)	7 (0.03)	0.231
Loop diuretic users, n (%)	10 (9.6)	24 (11)	0.732
Sglt-2-i users, n (%)	2 (1.9)	10 (0.05)	0.246
Hb g/dL	10.7 ± 2.1	12.6 ± 2	<0.001
TC, mg/dL	167 ± 70	199 ± 50	0.001
HDL, mg/dL	40.6 ± 14.7	50.6 ± 17	<0.001
LDL, mg/dL	98 ± 47	118 ± 39.6	0.004
TG, mg/dL	111 (85–165)	117 (89–192)	0.343
WBC, $10^3/\mu L$	10 (5.4–10.8)	6.4(4.6–8.8)	<0.001
Lymphocyte, $10^3/\mu L$, n (%)	7.1 (3.2–12.5)	15.1 (8.5–24.7)	<0.001

Table 2. *Cont.*

	Dead n: 104	Survived n: 221	*p* Value
Creatine, mg/dL	1.3 (0.8–2.4)	0.8 (0.6–1)	<0.001
AST, µ/L	45 (27–72)	34 (24–59)	0.003
ALT, µL/L	26 (15–41)	29(18–49)	0.176
LDH, µL/L	449 (335–592)	297 (229–413)	<0.001
Ferritin, mL/n	637 (273–1355)	276 (131–550)	<0.001
Hs-T (on admission), ng/L	21.5 (10–59)	5.6 (5.6–10)	<0.001
Hs-T (peak), ng/L	139 (38–629)	8 (5.6–19.5)	<0.001

Abbreviations: ACEI: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ASA: acetylsalicylic acid; BB: beta-blocker; BMI: body mass index; CAD: coronary artery disease; CCB: calcium-channel blocker; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease CVE: cerebrovascular event; ECG: electrocardiogram; Hb: haemoglobin; HDL: High-Density Cholesterol; HL: hyperlipidaemia; Hs-T: high-sensitivity troponin; ICU: Intensive Care Unit; LDL: Low-Density Cholesterol; MRA: Mineralocorticoid Receptor Antagonist; OAC: oral anticoagulant; SR: sinus rhythm; TC: total cholesterol; TG: triglyceride.

The thorax CT findings of the study population are outlined in Table 3. Moderate-to-severe involvement, according to the CO-RADS classification, was more frequent in deceased patients [85.5% (n = 89) vs. 70.5% (n = 156), (p = 0.003)]. The presence of aortic calcification and CAC was notably higher in deceased subjects ($p < 0.001$ for both), and the median Weston CAC score was 0 (0–3) in surviving patients and 3.5 (1–6.7) in deceased patients ($p < 0.001$). Furthermore, the EAT density was markedly higher [-82.7 ± 16 vs. -90.2 ± 16 HU, ($p < 0.001$)] in deceased patients.

Table 3. Comparison of imaging findings between dead and surviving patients.

	Dead n: 104	Survived n: 221	*p* Value
Thorax CT-CORADS 4–5, n (%)	89 (%85.5)	156 (%70.5)	0.003
Thorax CT-CACS	3.5 (1–6.7)	0 (0–3)	<0.001
Thorax CT-CACS +, n (%)	84 (%81)	100 (%45)	<0.001
Thorax CT—aortic calcification +, n (%)	86 (%82.7)	103 (%46.6)	<0.001
Thorax CT-EAT (HU)	-82.7 ± 15.9	-90.2 ± 16.5	<0.001

Abbreviations: CAC: coronary artery calcium score; EAT: epicardial adipose tissue; HU: Hounsfield Units.

Univariate logistic regression analysis was employed to determine the predictors of all-cause mortality, and the ROC curve analysis was utilised to ascertain the predictive values for significant numerical data (Figure 6). The best cut-off value was 67.5 years for age [AUC = 0.77 (95% CI: 0.72–0.83) p = <0.001], 12 g/dL for Hb [AUC = 0.747 (95% CI: 0.69–0.80) p = <0.001], −88.5 HU for EAT density [AUC = 0.63 (95% CI: 0.57–0.70) p = <0.001], and 9.5 ng/L for admission hs-T [AUC = 0.82 (95% CI: 0.77–0.87) p = <0.001]. The predictors of all-cause mortality are presented in Table 4. Among all these variables, an age > 67 (OR = 2.8, p = 0.012), an admission hs-T > 9.5 ng/L (OR = 7, p = 0.001), an admission heart rate > 100 bpm (OR = 4, p = 0.002), a saturation < 90% (OR = 3.5, p = 0.001), the presence of CAC and aortic calcification (OR = 3.9, p = 0.001), an Hb < 12 g/dL (OR = 3.8, $p < 0.001$), and not taking ASA at admission (OR = 15.1, $p < 0.001$) were found to be independent contributors to all-cause mortality.

The independent predictors were used to create the HEARRT-C score, and statistically significant mortality predictors were scored according to their OR values (Table 5). The AUC of the HEARRT-C score for predicting mortality was 0.91 (95% CI 0.87–0.94, $p < 0.0001$), and the best cut-off value was 5 with a sensitivity of 81% and specificity of 86% (Figure 7).

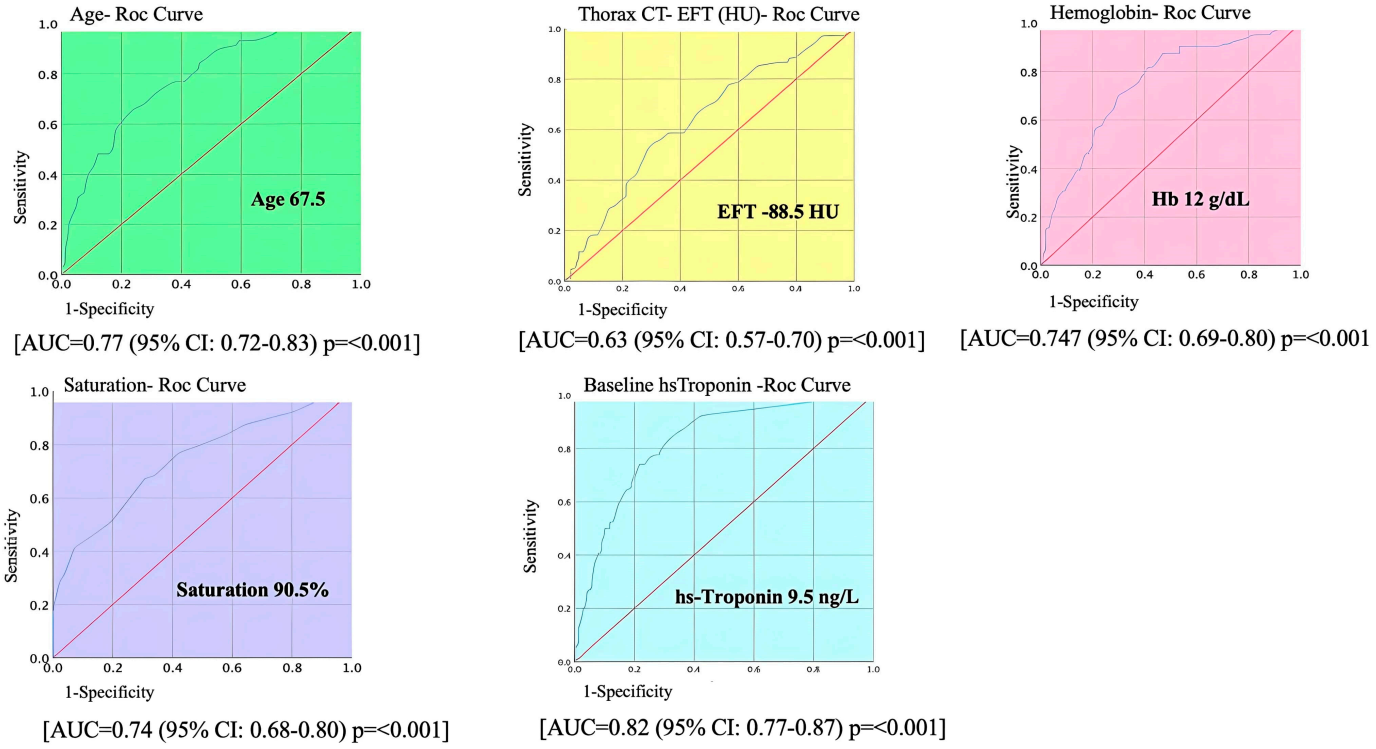


Figure 6. ROC curve analysis of age, saturation, Hb, EAT, and hs-T (on admission).

Table 4. Univariate and multivariate logistic regression analysis results.

	Univariate Logistic Regression Analysis			**Multivariate Logistic Regression Analysis**		
Variables	**OR**	**%95 CI**	***p***	**OR**	**%95 CI**	***p***
Age > 67 years	5.67	3.39–9.46	<0.001	2.8	1.25–6.24	0.012
HT	1.89	1.15–3.1	<0.011			
CKD	4.31	2.44–7.58	<0.001			
CAD	2.05	1.06–3.93	0.031			
ECG, non-SR	2.87	1.54–5.33	0.001			
Heart rate > 100 bpm	4.43	2.67–7.42	<0.001	4.02	1.78–9.06	0.001
Saturation < %90	4.63	2.81–7.63	<0.001	3.52	1.72–7.19	0.001
Thorax CT-CORADS 4–5	2.47	1.33–4.59	<0.001			
Thorax CT CAC + aortic calcification +	5.28	3.13–8.91	<0.001	3.85	1.69–8.78	0.001
Thorax CT-EAT > −88.5 HU	2.07	1.26–3.25	0.003			
Hb < 12 g/dL	5.32	3.19–8.86	<0.001	3.80	1.87–7.68	<0.001
Hs-T > 9.5 ng/L (on admission)	9.82	5.68–16.98	<0.001	6.03	2.90–12.52	<0.001
Not receiving ASA on admission	7.69	2.70–21.90	<0.001	15.61	4.46–54.62	<0.001

Abbreviations: ASA: acetylsalicylic acid; CAC: coronary artery calcium score; CAD: coronary artery disease; CKD: chronic kidney disease; EAT: epicardial adipose tissue; ECG: electrocardiogram; Hb: haemoglobin; Hs-T: high-sensitivity troponin; HU: Hounsfield Units.

Table 5. HEARRT-C score.

	HEARRT-C Score	
H	Haemoglobin < 12 g/dL	1 point
E	Elderly (age) > 67 years	1 point
A	ASA (not receiving)	2 point
R	Rate (heart rate > 100 bpm)	1 point
R	Respiration (saturation < 90%)	1 point
T	hsT ≥ 9.5 ng/L (on admission)	2 point
C	CACS + Aort calcification +	1 point
	Total points:	>5

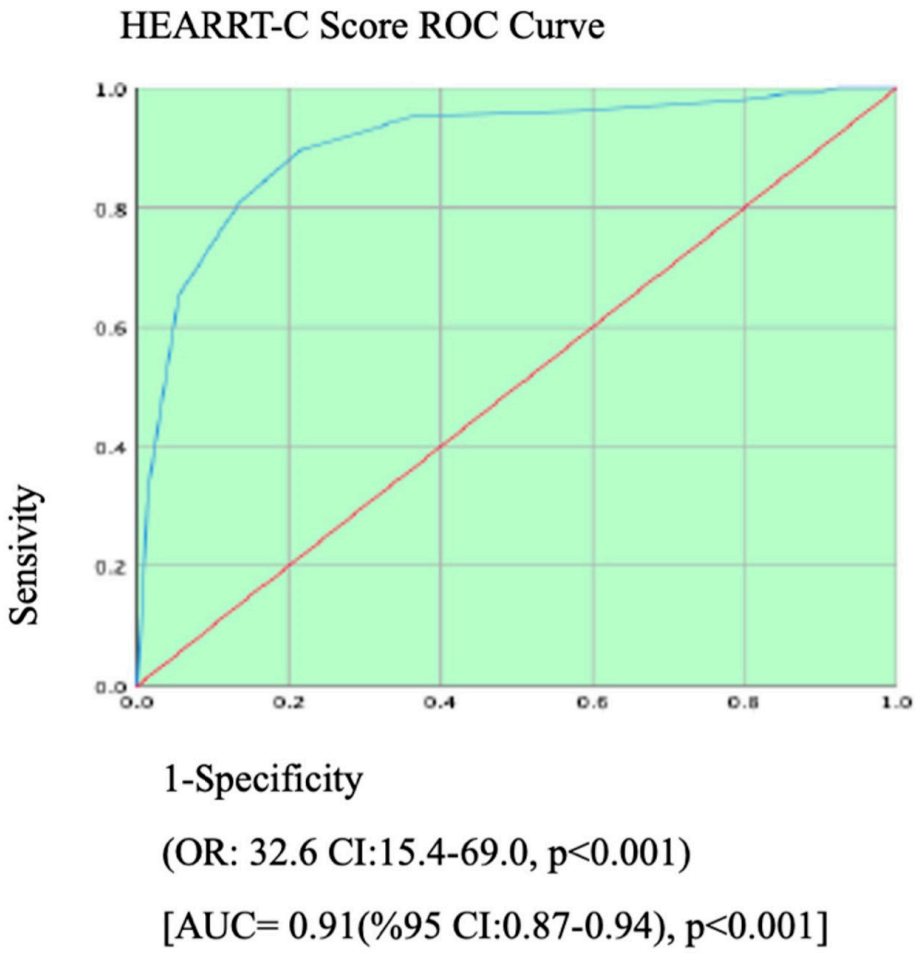


Figure 7. ROC curve analysis of HEARRT-C score.

4. Discussion

This study identified early to mid-term mortality predictors in hospitalised COVID-19 patients. We demonstrated that older age, decreased arterial oxygen saturation, tachycardia, anaemia, the presence of both coronary and aortic calcification, increased hs-T, and not receiving ASA were identified as independent predictors of all-cause mortality.

Advanced age (>67 years) may reflect a frail, high-risk patient population with multiple comorbidities. Low saturation (<90%) can be associated with moderate-to-severe lung involvement, increased mechanical ventilation, ICU requirement, and mortality. Tachycardia (heart rate >100 bpm) at admission can indicate hypoxemia, fever, anaemia, sepsis, and increased sympathetic activity. This adrenergic response may affect mortality through myocardial ischaemia and apoptosis and be linked with increased ICU needs and in-hospital events.

Anaemia (Hb < 12 g/dL), especially in high-risk patients, may increase mortality risk by failing to meet the peripheral tissues' increased oxygen demands during infection-induced hypermetabolic states [16]. CAC and aortic calcification may independently indicate systemic atherosclerosis and inflammation due to endothelial dysfunction, reflecting cumulative comorbidities and increasing all-cause mortality [17,18]. Additionally, calcifications can enhance viral replication and vascular damage through Renin–Angiotensin System (RAAS) activation [19].

Among other determinants, an admission hs-T level >9.5 ng/L and not receiving ASA at admission were the most critical mortality predictors. In patients with COVID-19, elevated hs-T levels can develop through various mechanisms. While ischaemic myocardial

injury (e.g., direct endothelial or vascular damage, spasm in coronaries, plaque rupture, microthrombosis) is observed less frequently, it is more often due to non-ischaemic myocardial injury (e.g., life-threatening hypoxia, pulmonary thromboembolism, sepsis, systemic inflammation cytokine storm, stress cardiomyopathy) or direct myocardial damage such as myocarditis. Therefore, hs-T may be a significant parameter in risk stratification, reflecting direct or indirect cardiac damage caused by COVID-19 [6,20].

ASA, which gained popularity during the 1918 Spanish flu pandemic, has been shown to reduce the ribonucleic acid (RNA) replication of the Middle East Respiratory Syndrome Coronavirus [21]. Additionally, Kristjan G. et al. showed that ASA reduces the development of acute respiratory distress syndrome (ARDS) in hospitalised viral or bacterial pneumonia cases [22]. The only study investigating the primary protective effects of ASA was conducted by Eugene Merzon et al. This study found that patients taking ASA were less likely to contract COVID-19 despite their older age (OR 0.71, CI: 0.52–0.99; $p = 0.041$) [18]. The possible protective mechanisms of low-dose ASA against COVID-19 might be explained by an enhanced antiviral immunity against RNA viruses through the inhibition of prostaglandin two biosynthesis and increased interferon induction. In the early stages, ASA can reduce viral replication and limit the release of pro-inflammatory mediators, preventing severe disease progression. In the late stages, where hyperinflammation and hypercoagulability emerge, ASA can decrease the severity of the cytokine storm and prevent fatal thrombosis through the acetylation of prothrombin and platelet membranes [21–23]. Despite ASA's reduced role in primary prevention due to increased bleeding risk, our study found that not taking ASA at hospital admission increased mortality in COVID-19 patients. Not taking ASA at admission contributed two points to the HEARRT-C score, making it one of the most essential mortality predictors.

In contrast, no statistically significant mortality association was found in patients taking oral anticoagulants (OACs). OACs, like many other drugs used in treatment, are metabolised through the glycoprotein (P-gp) pathway and cytochrome P450 (CYP) 3A4. Drug interactions that decrease the efficacy of OACs could be a mechanism explaining this outcome [24].

Although the WHO estimated an overall COVID-19 mortality rate of 2.1% as of February 2024, data specific to hospitalised patients remain scarce. Given the ongoing uncertainty surrounding long-term COVID-19 outcomes, our findings contribute meaningful insights. While antiviral treatments enhance clinical outcomes, their effectiveness may be compromised by emerging SARS-CoV-2 variants and limited global accessibility [25]. Our proposed scoring system could facilitate risk stratification before treatment initiation. Moreover, the anti-inflammatory properties of ASA, a widely available agent, may provide clinical benefits.

Scoring systems such as SIRS, NEWS, MEWS, 4C Mortality, and qSOFA, widely used for assessing sepsis and septic shock, have also been employed to predict COVID-19 mortality. Additionally, several novel scoring models have been developed specifically for COVID-19 patients. However, a detailed review of these systems reveals that none incorporate cardiac biomarkers such as hs-troponin or thoracic CT calcification data, despite cardiac complications being a significant contributor to COVID-19-related mortality.

Our proposed scoring system addresses this gap by integrating both cardiac biomarkers and imaging parameters, offering a more comprehensive risk stratification approach.

HEARRT-C demonstrated that cardiovascular imaging findings and cardiac biomarkers were more productive in mortality risk stratification than respiratory parameters in hospitalised COVID-19 patients. This result may indicate the impact of COVID-19's systemic involvement on mortality. The HEARRT-C score may aid in early risk assessment and the identification of high-risk cases. Additionally, demonstrating ASA's protective

effect in COVID-19 raises the question of reconsidering ASA in primary prevention for patients with high cardiovascular risk and infection vulnerability.

Limitations

The primary limitations of our study include the inability to accurately assess cardiovascular mortality, resulting in all-cause mortality being chosen as the primary endpoint, and the inability to conclude a genuine causal relationship due to the retrospective design. Our study was conducted at a single centre, resulting in a comparatively small patient population. Only hospitalised patients were included, excluding those followed up on an outpatient basis, and no control group existed. However, the effect of the HEARTT-C score on mortality was assessed using a post hoc power analysis with G*Power 3.1.9.7. When comparing the HEARTT-C scores of patients with and without mortality, the effect size was determined to be 0.8, and the power analysis result was 0.91. In conclusion, our study represents a preliminary report, and further validation through larger-scale, prospective studies is required.

Despite evaluating thoracic CT imaging findings with a radiologist, imaging artefacts due to technical issues could be misleading. Another drawback of our work is the relatively small number of subjects taking ASA at admission and its potential effect on statistical analysis. At the beginning of the COVID-19 pandemic, high-risk patients with multiple comorbidities or malignancies were predominantly hospitalised, which may not reflect the general population.

5. Conclusions

The HEARRT-C score is an easily accessible and practical scoring system that can help identify high-risk patients, potentially improving their management, especially in light of ongoing COVID-19-related mortality and ICU admissions even after the pandemic. In clinical practice, scoring systems developed for sepsis/septic shock and pneumonia are used in this patient group. This score is distinguished by including cardiac biomarkers and imaging findings, which are significant for determining cardiac mortality in these diseases. Moreover, while the role of ASA in primary prevention remains controversial, demonstrating its protective effect in COVID-19 could bring this discussion back to the forefront, especially for patients with high cardiovascular risk and susceptibility to infections.

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