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Cardiovascular and Thrombotic Manifestations of COVID-19 (SARS-CoV-2)

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**AMAZING
THINGS
ARE
HAPPENING
HERE**

Covid 19

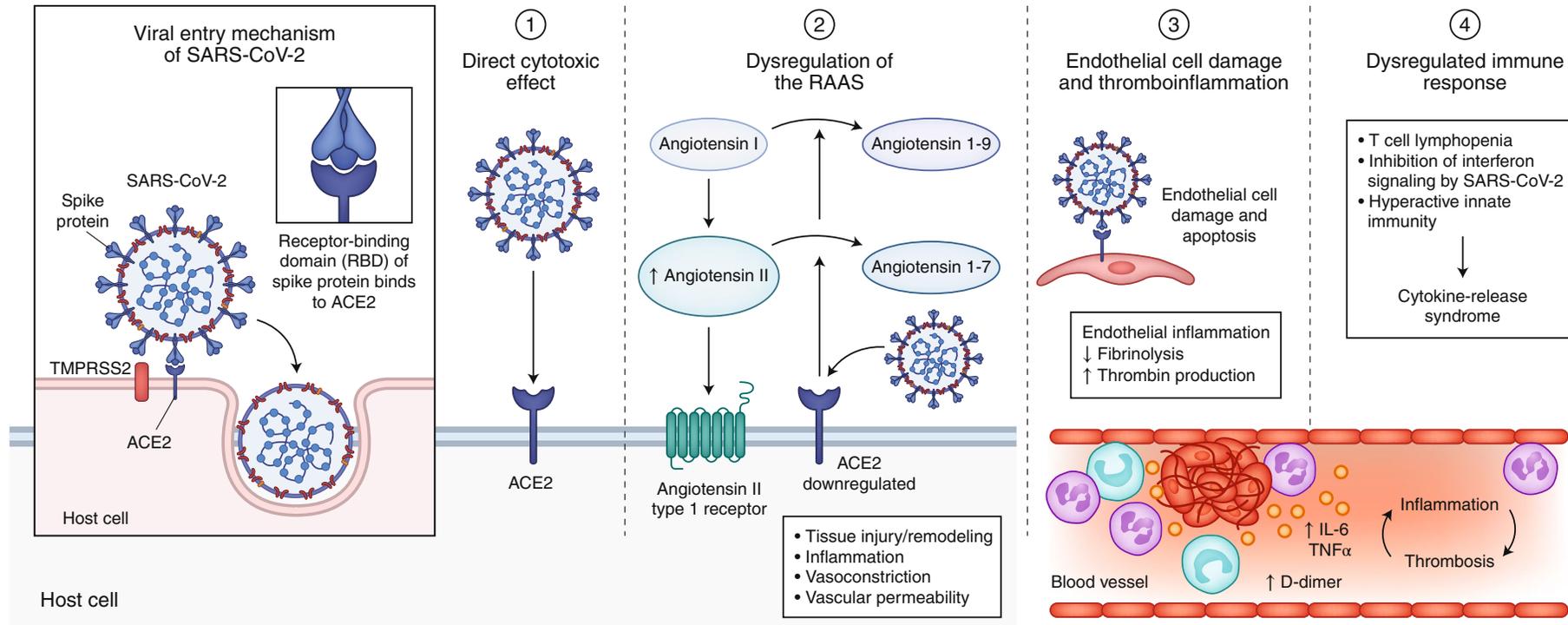


Fig. 1 | Pathophysiology of COVID-19. SARS-CoV-2 enters host cells through interaction of its spike protein with the entry receptor ACE2 in the presence of TMPRSS2 (far left). Proposed mechanisms for COVID-19 caused by infection with SARS-CoV-2 include (1) direct virus-mediated cell damage; (2) dysregulation of the RAAS as a consequence of downregulation of ACE2 related to viral entry, which leads to decreased cleavage of angiotensin I and angiotensin II; (3) endothelial cell damage and thromboinflammation; and (4) dysregulation of the immune response and hyperinflammation caused by inhibition of interferon signaling by the virus, T cell lymphodepletion, and the production of proinflammatory cytokines, particularly IL-6 and TNF α .

Extra Pulmonary Manifestations

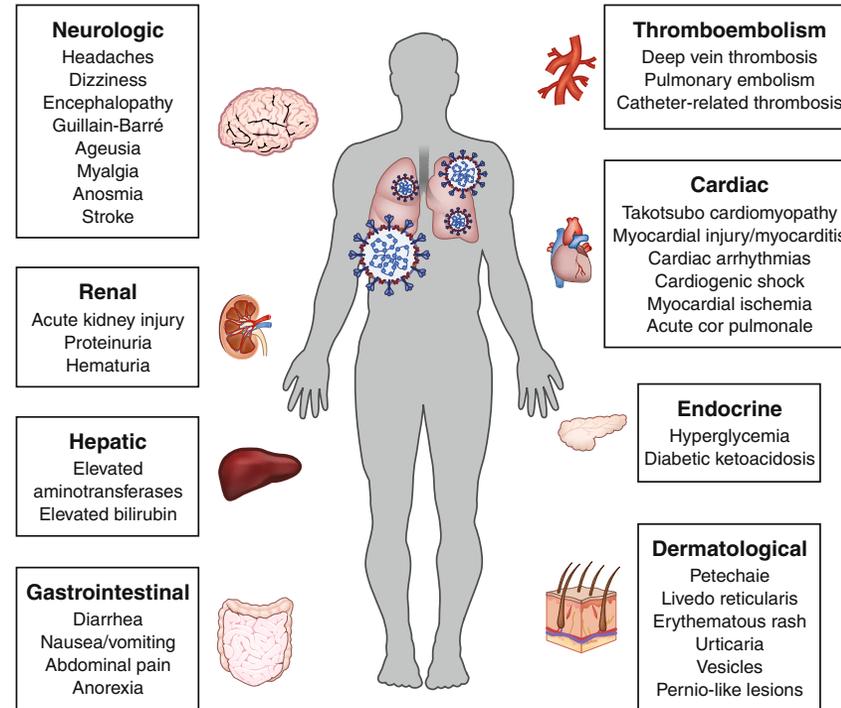
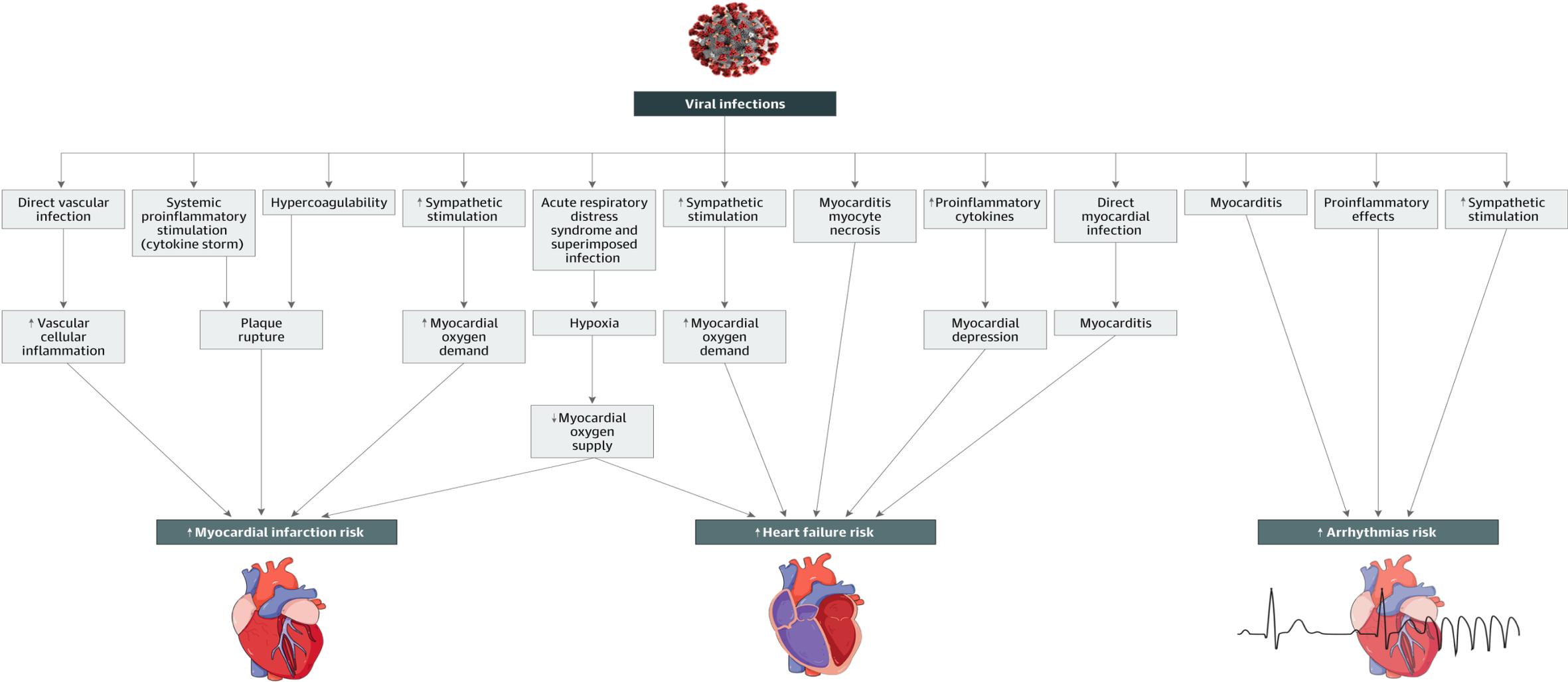


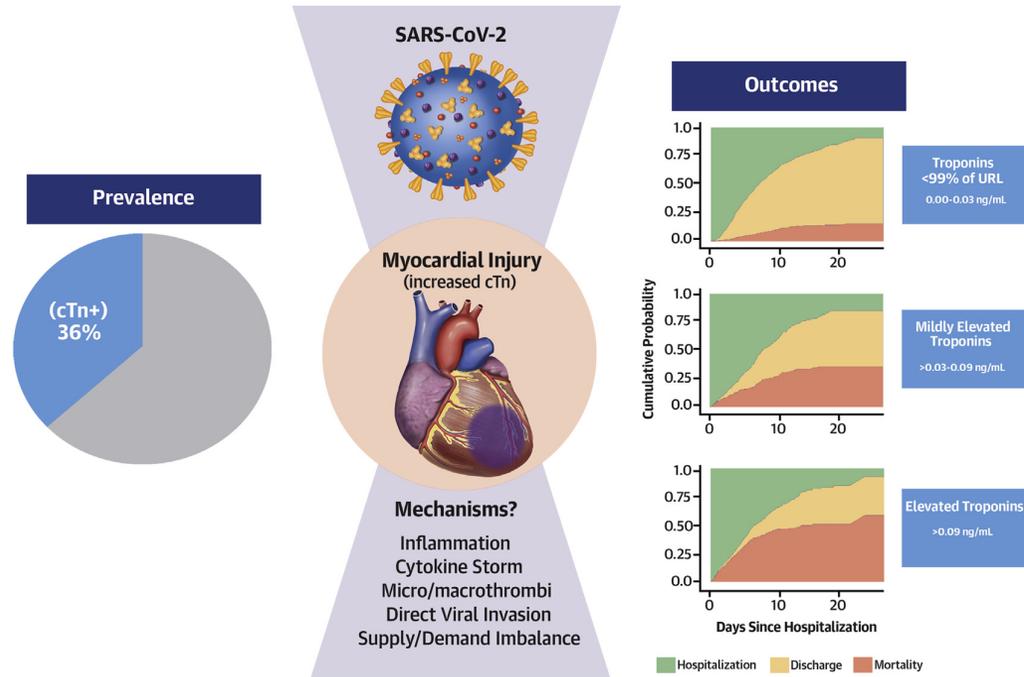
Fig. 2 | Extrapulmonary manifestations of COVID-19. The pulmonary manifestation of COVID-19 caused by infection with SARS-CoV-2, including pneumonia and ARDS, are well recognized. In addition, COVID-19 is associated with deleterious effects on many other organ systems. Common extrapulmonary manifestations of COVID-19 are summarized here.

Cardiovascular Manifestations of COVID-19



Cardiac Involvement

CENTRAL ILLUSTRATION Prevalence, Potential Mechanisms, and Impact of Myocardial Injury in Coronavirus Disease-2019



Lala, A. et al. J Am Coll Cardiol. 2020;76(5):533-46.

Myocardial injury reflected by troponin concentrations above the upper reference limit (URL) of 0.03 ng/ml was present in 36% of patients hospitalized with coronavirus disease-2019 (COVID-19). Troponin levels among patients hospitalized with COVID-19 were generally <1.0 ng/ml. Even small amounts of myocardial injury (e.g., troponin I >0.03 to 0.09 ng/ml, n = 455 [16.6%]) were associated with death (adjusted HR: 1.75; 95% confidence interval: 1.37 to 2.24) while greater amounts (e.g., troponin I >0.09 ng/dl, n = 530 [19.4%]) were associated with more pronounced risk for death (adjusted HR: 1.77; 95% confidence interval: 1.39 to 2.26; p < 0.001). Troponin elevation in the setting of acute COVID-19 may primarily reflect nonischemic or secondary myocardial injury, but the true mechanism remains unknown. SARS-CoV-2 = severe acute respiratory syndrome-coronavirus-2.

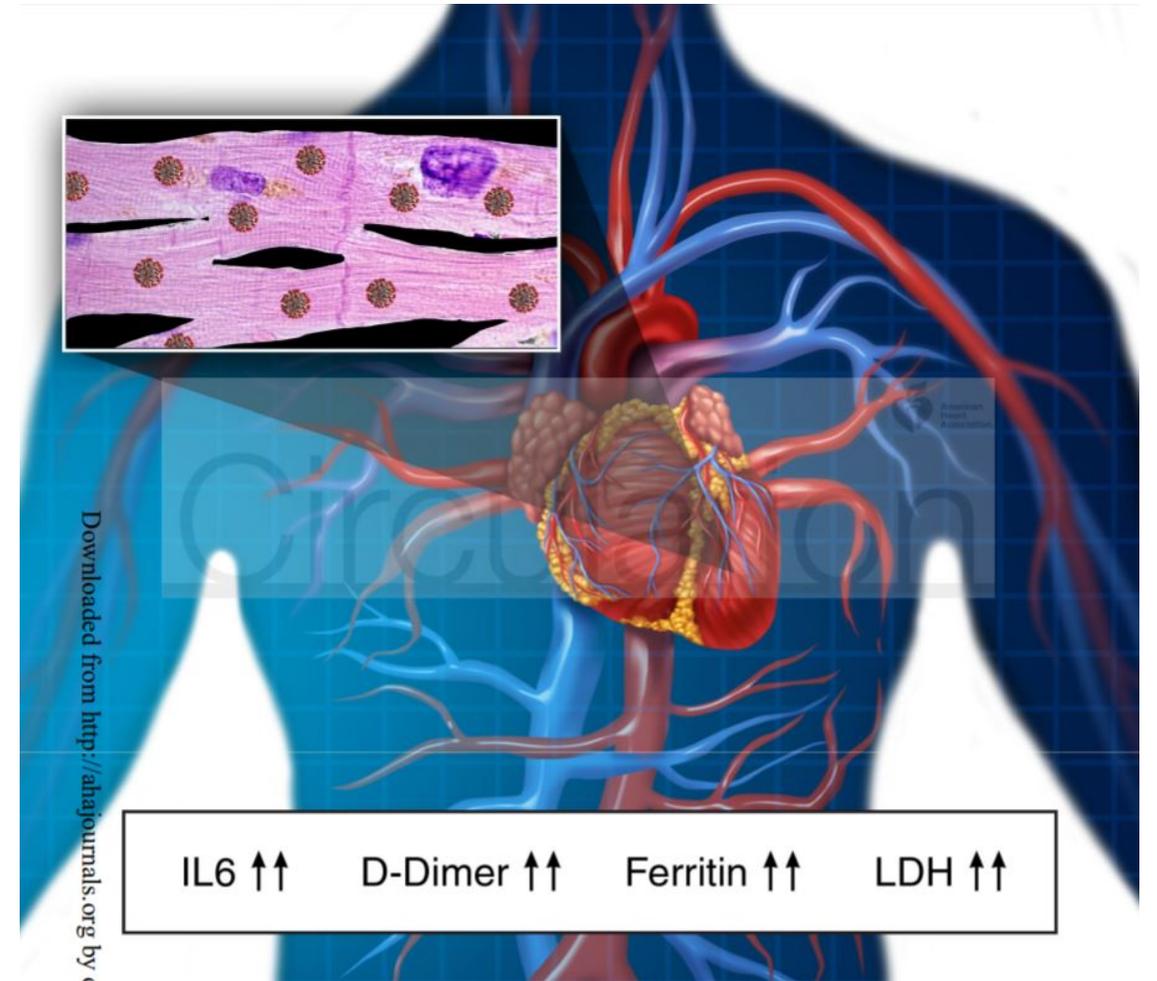
TABLE 1 Published Studies Worldwide Demonstrating Association Between Myocardial Injury Diagnosed by Troponin Elevation and the Association With COVID-19-Associated Mortality

Location	N	Patient Acuity	Assay Used	HR (95% CI) for Death	Prevalence in Nonsurvivors vs. Survivors	Ref. #
Wuhan, China	671	Severe	hs-cTnI	4.56 (1.28-16.28)	75.8% vs. 9.7%	(4)
Wuhan, China	416	Hospitalized	hs-cTnI	4.26 (1.92-9.49)	51.2% vs. 4.5%	(5)
Wuhan, China	191	Hospitalized	hs-cTnI	80.1 (10.3-620.36)	46% vs. 1%	(6)
Seattle, United States	24 (13 with measured troponin)	Severe	Troponin (not otherwise specified)		50% (n = 1 of 2) vs. 45% (n = 5 of 11)	(9)
Northern Italy	53	Hospitalized with pre-existing CVD	hs-cTnT		100% vs. 74%	(10)
New York City, United States	2,736	Hospitalized	Troponin I	Low (0.03-0.09 ng/ml): 1.75 (1.37-2.24) High (>0.09 ng/ml): 3.03 (2.42-3.80)	60% (>0.09 ng/ml) vs. 35% (0.03-0.09 ng/ml) vs. 15% (<0.03 ng/ml) (estimated from Figure 1 of Lala et al.)	(7)

CI = confidence interval; COVID-19 = coronavirus disease-2019; CVD = cardiovascular disease; HR = hazard ratio; hs-cTnI = high-sensitivity cardiac troponin I; hs-cTnT = high-sensitivity cardiac troponin T.

Myocardial Injury

- Myocardial injury during COVID-19 can be explained by two mechanisms
 - Caused by the associated cytokine storm manifested by elevated levels of IL-6, ferritin, LDH, and D-dimer.
 - Myocardial dysfunction from the direct effect of SARS-CoV-2 on the heart.



Reports of SARS-COV-2 genome in myocardial tissue

- 104 patients with suspected COVID-19 associated myocarditis or unexplained HF, EMB demonstrated:

Group	All patients
Number of patients, <i>n</i> (%)	104 (100)
Men, <i>n</i> (%)	79 (76)
Age at diagnosis, mean \pm SD (years)	57.9 \pm 16.4
LVEF at diagnosis, mean \pm SD (%)	33.7 \pm 14.6
Diagnosis, <i>n</i> (%)	
• Active myocarditis	14 (13.4)
• Inflammatory cardiomyopathy	34 (32.6)
• Borderline myocarditis	3 (2.9)
• Dilated cardiomyopathy	43 (41.3)
• Amyloidosis	10 (9.6)

Biopsy

Table 2 Characteristics of patients

Patient	1	2	3	4	5
Age at diagnosis (years)	48	62	60	36	39
Clinical suspected diagnosis	Acute myocarditis	Unexplained heart failure	Unexplained heart failure	Inflammatory cardiomyopathy	Acute myocarditis
Diagnosis	Active myocarditis	Inflammatory cardiomyopathy	Inflammatory cardiomyopathy	Inflammatory cardiomyopathy	Borderline-myocarditis
Sex	M	M	F	M	M
LVEF at diagnosis (%)	22	40	60	25	55
Laboratory parameters:					
High sensitive Troponin (pg/mL)	3264	-	83	56	379
BNP (pg/mL)	12 232	-	113	258	109
EMB analysis:					
Myocyte diameter (μm)	18	18	32	22	19
CD3+ count in EMB (cells/ mm^2)	106.98	7.0	20.54	4.97	18.74
CD45RO+ count in EMB (cells/ mm^2)	156.23	14.0	96.15	61.47	162.38
LFA-1+ count in EMB (cells/ mm^2)	83.15	-	24.36	16.95	102.6
Mac-1+ count in EMB (cells/ mm^2)	155.34	39,5	91.56	49.09	154.35
Perforin+ count in EMB (cells/ mm^2)	1.79	-	1.74	0.00	4.01
CD54+ count in EMB (%Area Fraction)	6.42	-	1.91	1.90	4.05
HLADR+ count in biopsy (%Area Fraction)	7.25	0,5	3.78		7.14

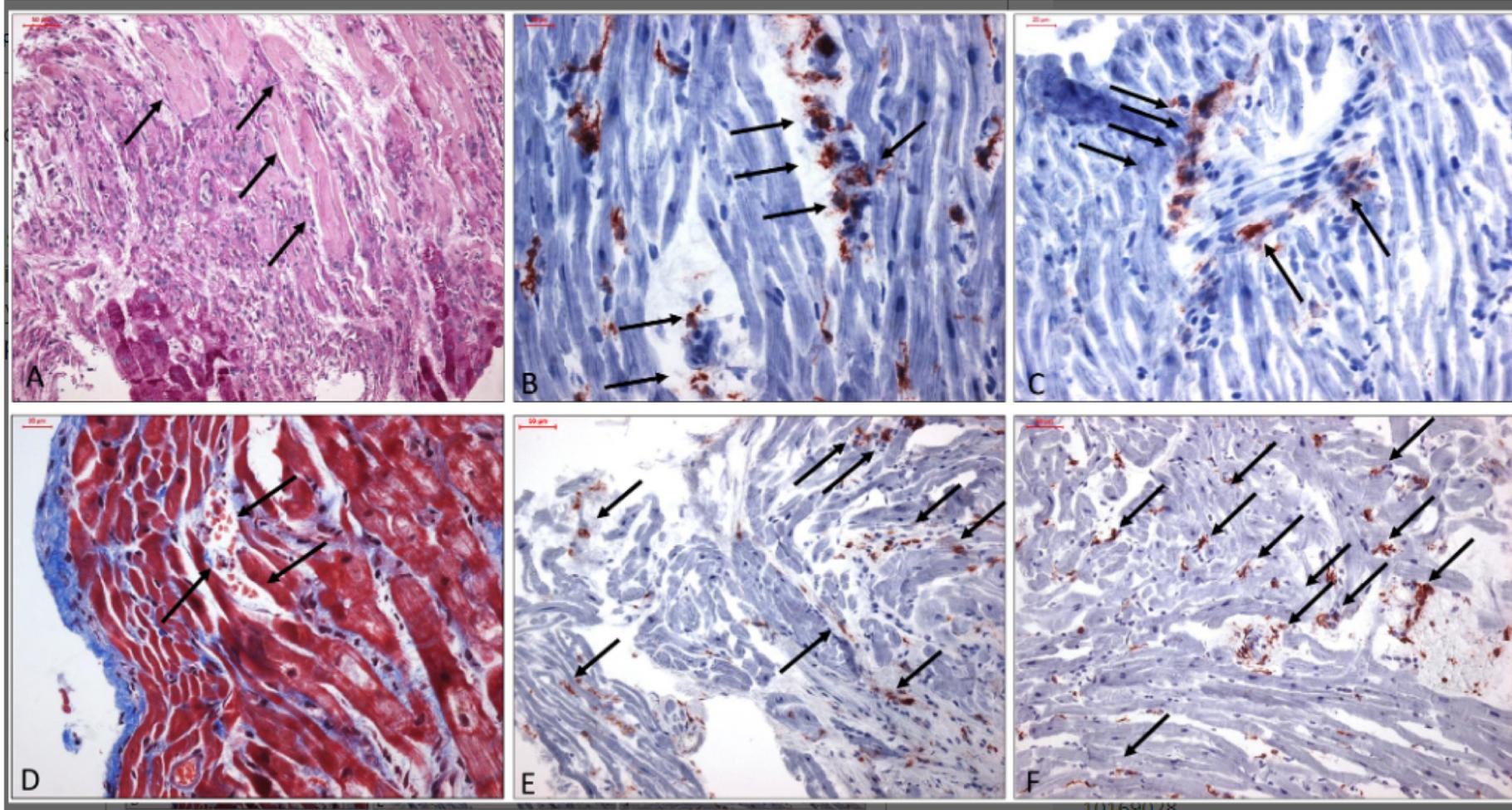


Table 4 LVEF among patients with COVID-19, stratified by normal or elevated hs-cTnT and normal or elevated NT-proBNP before undergoing a transthoracic echocardiogram

Cardiac biomarkers	Normal value before TTE, <i>n</i> (%)	Elevated value before TTE, <i>n</i> (%)	Unknown, <i>n</i> (%)
hs-cTnT	(<i>n</i> = 23)	(<i>n</i> = 46)	(<i>n</i> = 3)
Normal LVEF (>50%)	16 (69.6)	24 (52.2)	3 (100)
Reduced LVEF (≤50%)	4 (17.4)	21 (45.7)	—
Unable to assess	3 (13)	1 (2.2)	—
NT-proBNP	(<i>n</i> = 27)	(<i>n</i> = 21)	(<i>n</i> = 24)
Normal LVEF (>50%)	19 (70.4)	10 (47.6)	14 (58.3)
Reduced LVEF (≤50%)	5 (18.5)	11 (52.4)	9 (37.5)
Unable to assess	3 (11.1)	0 (0)	1 (4.2)

Normal hs-cTnT was defined as ≤22 ng/L, elevated hs-cTnT was defined as >22 ng/L, normal NT-proBNP was defined as <1,800 pg/mL, and elevated NT-proBNP was defined as ≥1,800 pg/mL.

Cardiac MRI

Table 1. Patient Characteristics, Cardiac Magnetic Resonance (CMR) Imaging Findings, and Blood Test Results on the Day of CMR Examination

Characteristic	Median (IQR)			P value
	COVID-19 (n = 100)	Healthy controls (n = 50)	Risk factor-matched controls (n = 57)	
Patient characteristics				
Age, y	49 (45-53)	48 (43-52)	49 (46-52)	.61
Male, No. (%)	53 (53)	25 (50)	28 (52)	.95
BMI ^a	25 (23-28)	23 (22-26) ^b	27 (24-29)	<.001
Hypertension, No. (%)	22 (22)	0	14 (24)	.77
Diabetes, No. (%)	18 (18)	0	12 (22)	.64
Hypercholesterolemia, No. (%)	22 (22)	0	13 (23)	.89
Known CAD, No. (%)	13 (13)	0	9 (16)	.60
Smoking, No. (%)	22 (22)	9 (18)	11 (19)	.66
COPD or asthma, No. (%)	21 (21)	0	13 (23)	.77
Blood pressure, mm Hg				
Systolic	129 (125-133)	122 (118-124) ^b	130 (127-135)	<.001
Diastolic	80 (76-83)	75 (73-78) ^b	79 (74-83)	.03
Heart rate, beats per min	67 (64-72)	64 (60-68)	67 (64-70)	.10
SCORE, %	4.0 (2.3-6.0)	NA	4.0 (3.1-6.2)	.92

Results!

Table 1. Patient Characteristics, Cardiac Magnetic Resonance (CMR) Imaging Findings, and Blood Test Results on the Day of CMR Examination

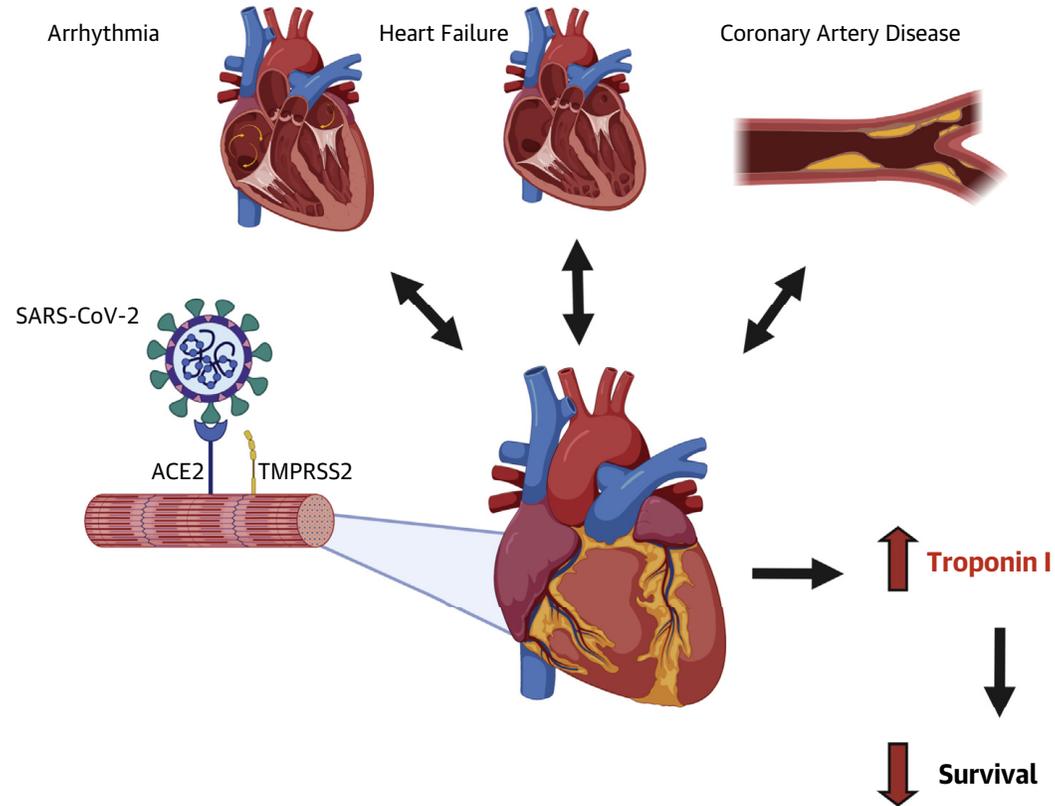
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Patient characteristics				
Age, y	49 (45-53)	48 (43-52)	49 (46-52)	.61
Male, No. (%)	53 (53)	25 (50)	28 (52)	.95
BMI ^a	25 (23-28)	23 (22-26) ^b	27 (24-29)	<.001
Hypertension, No. (%)	22 (22)	0	14 (24)	.77
Diabetes, No. (%)	18 (18)	0	12 (22)	.64
Hypercholesterolemia, No. (%)	22 (22)	0	13 (23)	.89
Known CAD, No. (%)	13 (13)	0	9 (16)	.60
Smoking, No. (%)	22 (22)	9 (18)	11 (19)	.66
COPD or asthma, No. (%)	21 (21)	0	13 (23)	.77
Blood pressure, mm Hg				
Systolic	129 (125-133)	122 (118-124) ^b	130 (127-135)	<.001
Diastolic	80 (76-83)	75 (73-78) ^b	79 (74-83)	.03
Heart rate, beats per min	67 (64-72)	64 (60-68)	67 (64-70)	.10
SCORE, %	4.0 (2.3-6.0)	NA	4.0 (3.1-6.2)	.92
CMR findings				
LVEF, %	56 (54-58)	60 (58-62) ^b	61 (58-64) ^b	<.001
LVEDV index, mL/m ²	86 (81-89)	80 (76-84) ^b	75 (71-79) ^b	<.001
LV mass index, g/m ²	51 (47-56)	47 (45-54) ^b	53 (50-55) ^b	.001
RVEF, %	56 (52-59)	60 (56-63) ^b	59 (56-62) ^b	.004
Native T1, ms				
Native T1, ms	1130 (1119-1150)	1077 (1065-1089) ^b	1109 (1101-1119) ^b	<.001
Abnormal native T1, No. (%)	73 (73)	3 (6) ^b	23 (40) ^b	<.001
Significantly abnormal native T1 (upper tertile), No. (%)	38 (38)	0 ^b	9 (16) ^b	<.001
Native T2, ms				
Native T2, ms	39 (37-40)	35 (34-36) ^b	36 (35-37) ^b	<.001
Abnormal native T2, No. (%)	60 (60)	2 (4) ^b	5 (9) ^b	<.001
Significantly abnormal native T2 (upper tertile), No. (%)	22 (22)	0 ^b	1 (2) ^b	<.001
LGE, No. (%)				
LGE, No. (%)				
Myocardial	32 (32)	0 ^b	9 (17) ^b	<.001
Nonischemic	20 (20)	0 ^b	4 (7) ^b	<.001
Pericardial	22 (22)	0 ^b	8 (15) ^b	<.001
Pericardial effusion (>10 mm), No. (%)	20 (20)	0 ^b	8 (15) ^b	<.001
Blood test results				
High-sensitivity CRP, mg/dL	0.24 (0.16-0.31)	0.11 (0.09-0.14) ^b	0.12 (0.07-0.17) ^b	<.001
hsTnT, pg/mL	5.6 (4.1-6.6)	3.2 (3.0-3.5) ^b	3.9 (3.2-4.5) ^b	<.001
Detectable hsTnT (≥3 pg/mL), No. (%)	71 (71)	11 (22) ^b	31 (57) ^b	<.001
Significantly elevated hsTnT (≥13.9 pg/mL), No. (%)	5 (5)	0 ^b	0 ^b	.06
NT-proBNP, pg/mL	69 (53-82)	48 (41-56) ^b	58 (50-66)	.02

Abbreviations: BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; hsTnT, high-sensitivity troponin T; IQR, interquartile range; LGE, late gadolinium enhancement; LV, left ventricle; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; NA, not applicable; NT-proBNP, N-terminal pro-B-type natriuretic peptide; RVEF, right ventricular ejection fraction; SCORE, Systematic Coronary Risk Evaluation.

^a Calculated as weight in kilograms divided by height in meters squared.

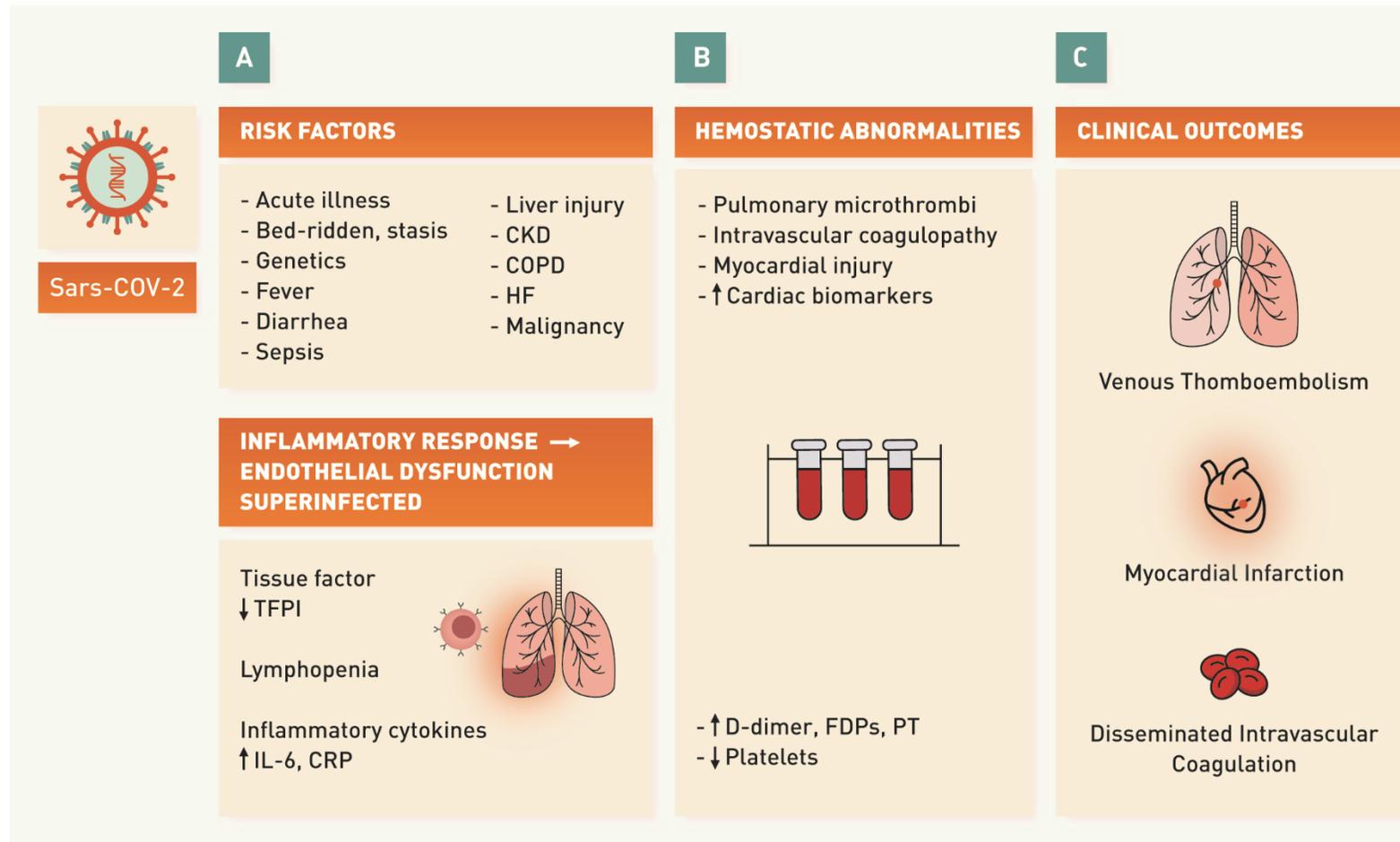
^b Bonferroni post hoc test for the difference vs COVID-19 group; P < .05.

FIGURE 1 Interplay of Cardiovascular Disease and SARS-CoV-2



The interplay of pre-existing cardiovascular disease (arrhythmia, heart failure, coronary artery disease) and severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) (pictured with spike protein binding to angiotensin-converting enzyme 2 receptor) on the heart. ACE2 = angiotensin-converting enzyme 2; TMPRSS2 = transmembrane protease, serine 2.

Mechanisms of Coagulopathy and Pathogenesis of Thrombosis in COVID-19



Epidemiology of Thrombotic Disease in COVID-19

- Limited data available suggests a high incidence of thrombotic complications in patients with COVID-19
 - Rates may exceed 20-30% in infected patients who are critically ill
- Patients who develop thrombotic complications have higher burden of clinical comorbidities as well as inflammatory and hemostatic laboratory derangements
- Cui et al (20/81 or 25% of ICU patients with VTE [diagnosed by CTAPE, venous US], 8 of whom died)
 - None of these patients received prophylactic anticoagulation

Table 2 Characteristics between the VTE and non-VTE groups (n = 81).

Characteristics	Normal range	VTE (n=20)	Non-VTE (n=61)	P-value
Age (years)	-	68.4 ± 9.1	57.1 ± 14.3	<0.001
Leucocytes ($\times 10^9/L$)	3.5-9.5	7.8 ± 3.1	6.6 ± 2.6	0.120
Lymphocytes ($\times 10^9/L$)	1.1-3.2	0.8 ± 0.4	1.3 ± 0.6	<0.001
Platelets ($\times 10^9/L$)	125.0-350.0	246.6 ± 110.6	248.8 ± 111.7	0.938
Haemoglobin (g/L)	115.0-150.0	123.2 ± 16.5	125.3 ± 16.7	0.633
APTT (s)	27.0-45.0	39.9 ± 6.4	35.6 ± 4.5	0.001
Prothrombin time (s)	11.0-16.0	15.4 ± 1.0	15.6 ± 1.0	0.465
D-dimer ($\mu g/mL$)	0.0-0.5	5.2 ± 3.0	0.8 ± 1.2	<0.001

APTT, activated partial thromboplastin time.

Pulmonary Embolism in COVID-19

- Study on PE by Poissy and colleagues on first 107 patients admitted to ICUs with COVID-19 in France
- High rate of PE (22/107 or 20.6%) within median time from ICU of 6 days
- At the time of diagnosis, 20/22 (91%) of these patients were on guideline directed prophylaxis
- Events compared between individuals admitted to ICU during same interval in 2019

Table. Number of CT Pulmonary Angiography performed for suspicion of PE, Number and main characteristics of Pulmonary Embolism (PE) Events in Intensive Care Unit from COVID-19 pandemic period by comparison to the same period in 2019 and to influenza patients in 2019

	Study period		
	2019, February 27 th to March 31 th (all ICU patients*, n=196)	2019, 1st January to 31 th December (Influenza ICU patients (PCR+), n=40)	2020, February 27 th to March 31 th (COVID-19 ICU patients, (PCR+), n=107)
Number of chest CT scans, n (%)	50 (25.5)	20 (50.0)	36 (33.6)
Number of CTPA, n (%)	30 (15.3)	17 (42.5)	34 (31.8)
Number of CTPA performed for a PE diagnosis, n (%)	20 (10.2)	8 (20.0)	34 (31.8)
Number of PE cases (%)	12 (6.1)	3 (7.5)	22 (20.6)**
Bilateral, n (%)	8 (66.6)	0 ***	8 (40.0) §
Proximal, n (%)	2 (16.6)	0 ***	2 (10.0) §
Segmental, n (%)	6 (50.0)	0 ***	11 (55.0) §
ARDS, n (%)	14 (7.1)	15 (37.5)	67 (62.6)
Intubation, n (%)	84 (42.9)	17 (42.5)	67 (62.6)
Doppler ultrasound, n (%)	12 (6.1)	2 (5.0)	8 (7.5)
DVT, n (%)	9 (4.6)	1 (2.5)	5 (4.7)
Patients with Pulmonary Embolism			
Age, years, median (range)	66 (30 to 72)	71 (57 to 72)	57 (29 to 80)
Men, n (%)	8 (66.7)	2 (66.7)	13 (59.1)
Body mass index, median (range)	29 (18 to 42)	26 (16 to 52) §§	30 (22 to 53)
SOFA at admission, median (range)	8 (1 to 16)	2 (1 to 9)	4 (0 to 14)
SAPS II at admission, median (range)	53 (23 to 69)	41 (34 to 65)	40 (18 to 78)
ARDS, n (%)	5 (41.7)	2 (66.7)	17 (77.3)
Intubation, n (%)	8 (66.7)	3 (100.0)	17 (77.3)
DVT associated to PE, n (%)	7 (58.3)	1 (33.4)	3 (13.6)

Thrombotic Disease in COVID-19

- Study from Netherlands by Klok and colleagues of 184 COVID-19 patients admitted to ICUs
- All patients received prophylaxis with LMWH (nadroparin)
- Overall mortality rate of 8%
- Cumulative incidence of any thrombotic event was 31% (95%CI 20-41%)
- Age and coagulopathy were identified as independent predictors of thrombotic events

Table 1

Characteristics of included patients.

Age (Mean, standard deviation)	64 (12)
Male sex (number, %)	139 (76)
Body weight (mean, standard deviation)	87 (16)
Active cancer (number, %)	5 (2.7)
Coagulopathy during admission ^a (n, %)	70 (38)
Therapeutic anticoagulation at admission (n, %)	17 (9.2)
Renal replacement therapy during admission (n, %)	23 (13%)

^a Defined as: spontaneous prolongation of the prothrombin time (PT) > 3 s or activated partial thromboplastin time (APTT) > 5 s.

Table 3

Description of thrombotic complications.

Type of event	Number of cases	Relevant details
Pulmonary embolism	25	- 18 cases with at least PE in segmental arteries, 7 cases PE limited to subsegmental arteries
Other venous thromboembolic events	3	- 1 proximal deep-vein thrombosis of the leg - 2 catheter related upper extremity thrombosis
Arterial thrombotic events	3	- All ischemic strokes

Note: acute pulmonary embolism was diagnosed with CT-pulmonary angiography, deep vein thrombosis/upper extremity vein thrombosis was diagnosed with ultrasonography, strokes were diagnosed with CT.

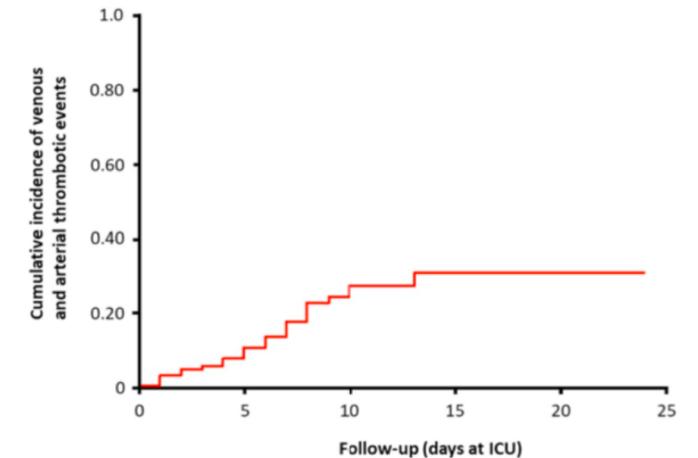
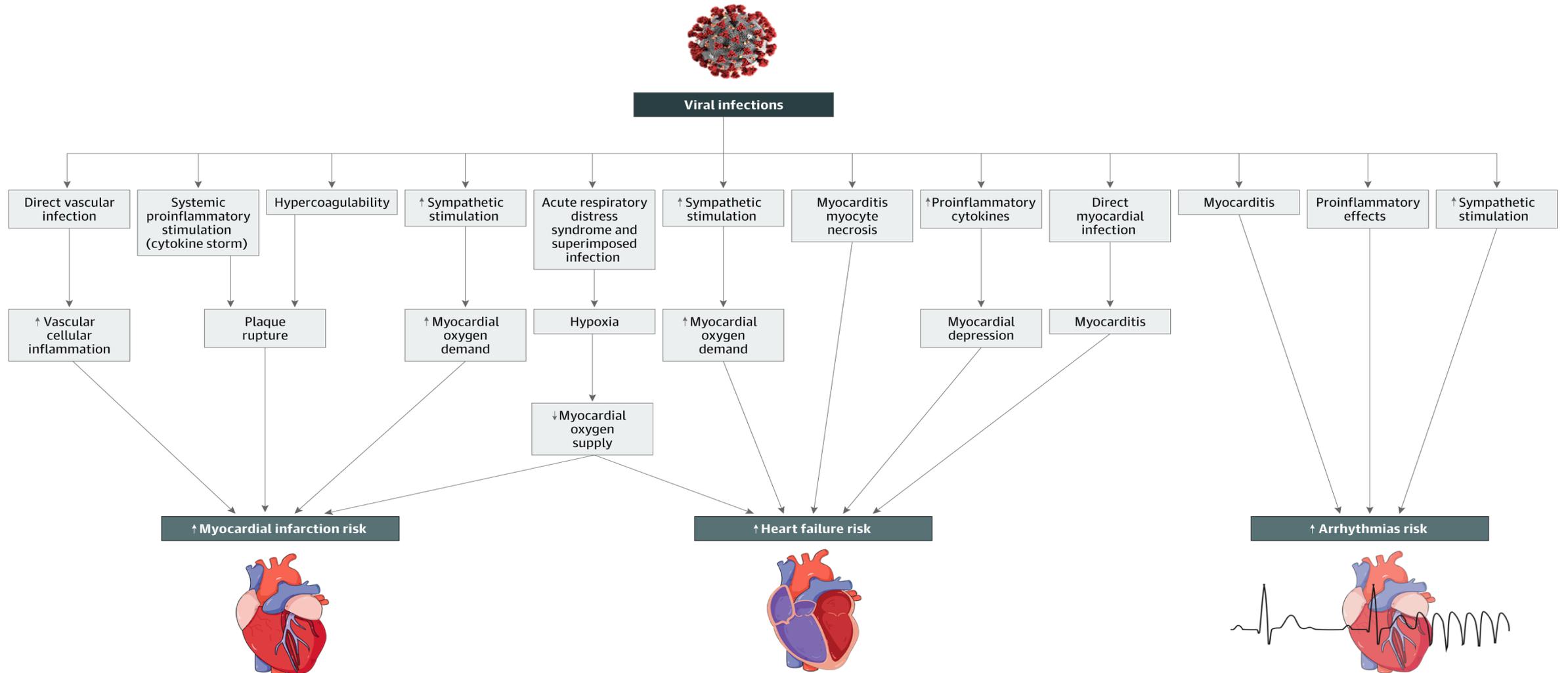


Fig. 1. Cumulative incidence of venous and arterial thrombotic complications during the course of intensive care unit admission of patients with proven COVID-19 pneumonia.

Cardiovascular Manifestations of COVID-19

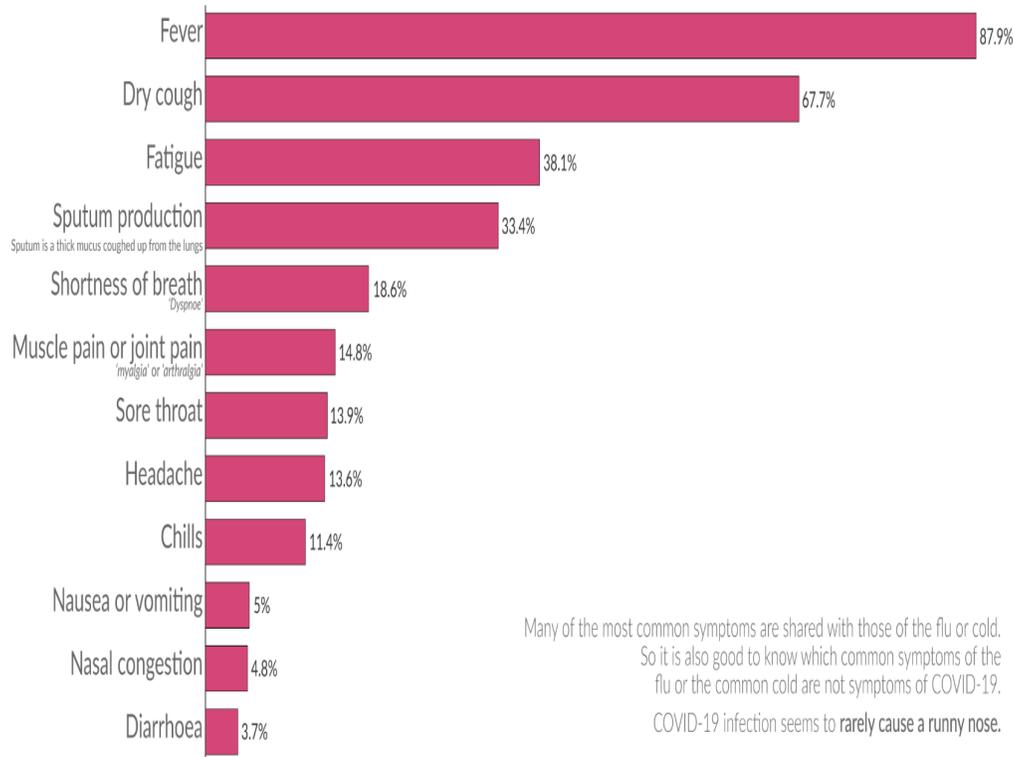


**THANK YOU
BE SAFE**

Aug 2020

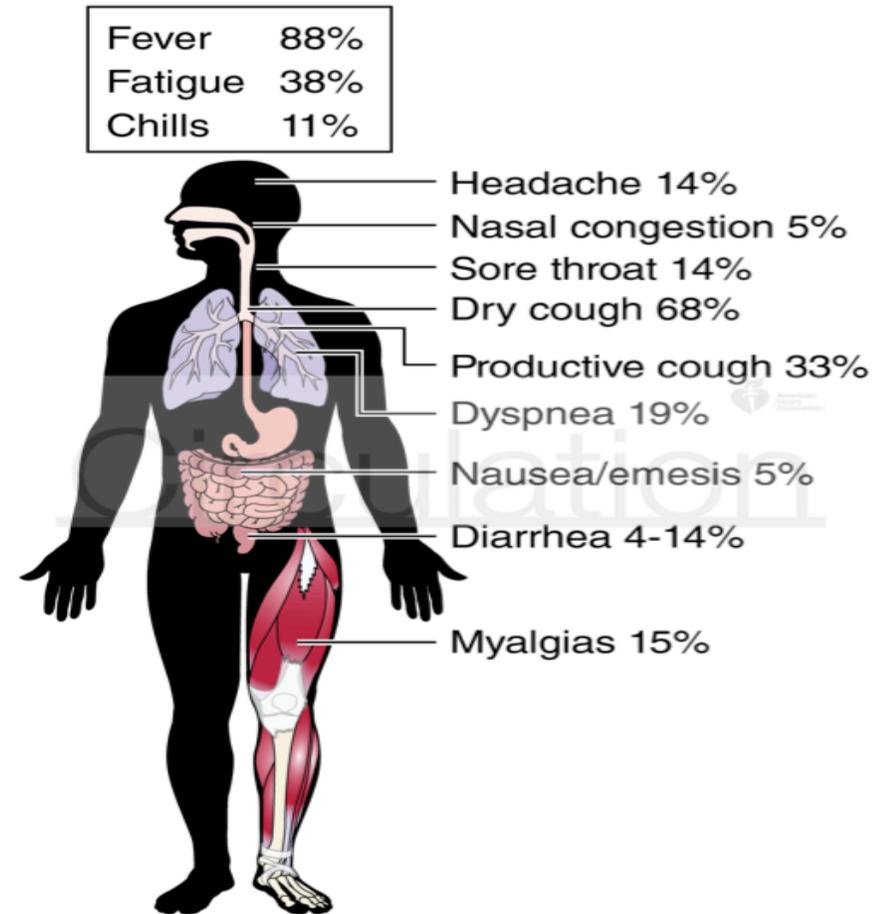


Symptoms



Many of the most common symptoms are shared with those of the flu or cold. So it is also good to know which common symptoms of the flu or the common cold are not symptoms of COVID-19. COVID-19 infection seems to rarely cause a runny nose.

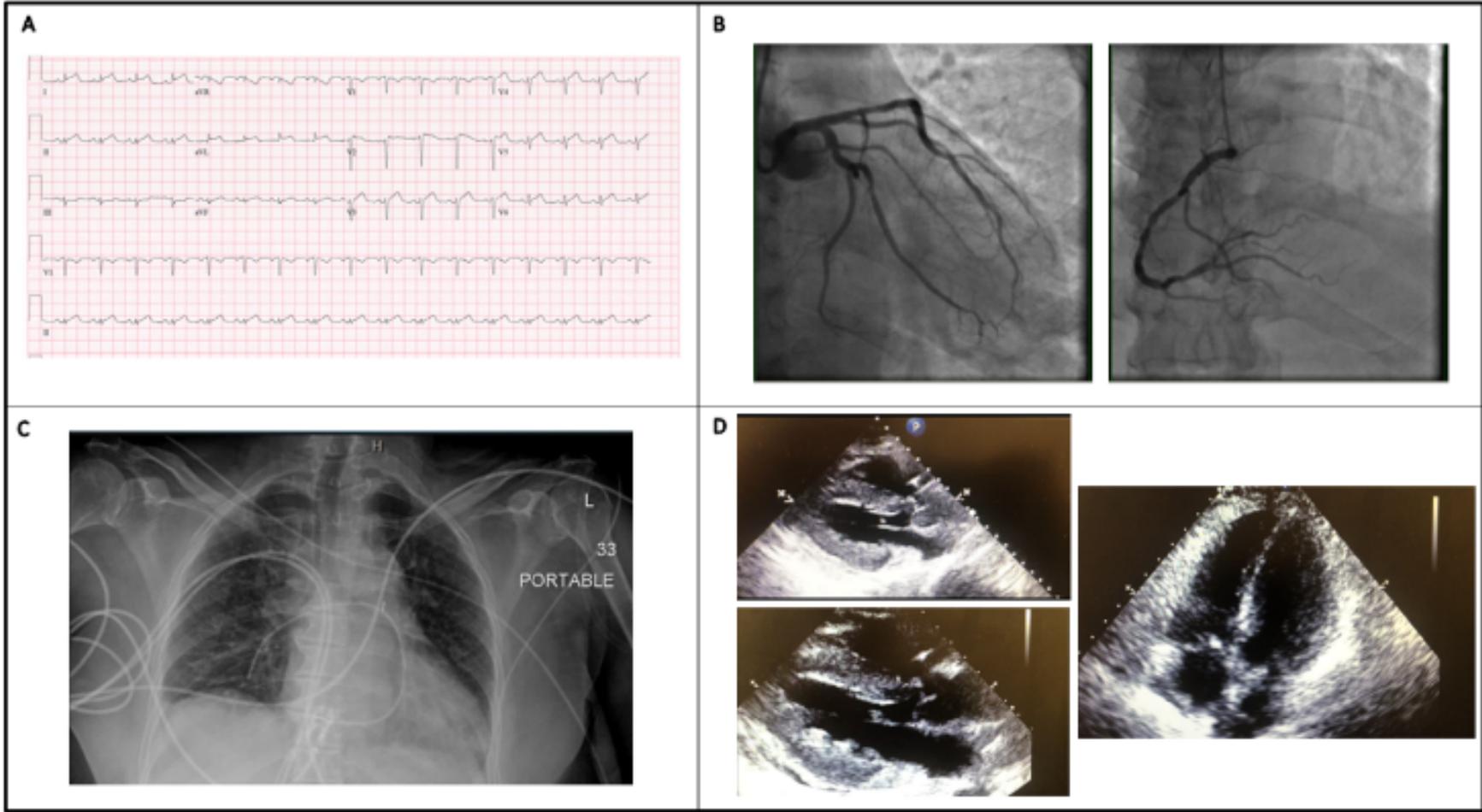
Data source: World Health Organization (2020). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Symptoms in fewer than 1% are not shown.



<https://ourworldindata.org/coronavirus>

Case Presentation

- 64 y/o female with history of hypertension and hyperlipidemia
- Presents with persistent chest pressure for two days
 - Denies dyspnea, cough, fever, chills or diarrhea. Denies recent travel or sick contacts.
- Vitals: BP 130/80, HR 98/min, O2 saturation 100% on 2 liters NC
- Exam: Mild distress, mild tachycardia, no evidence of volume overload or low output
- TnI 18.6, CK-MB 70 pBNP 5766



Prognostic Implication Of Myocardial Injury

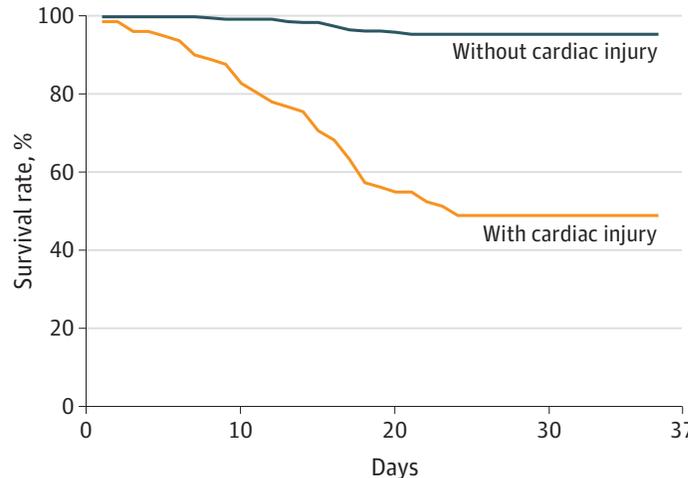
Table 2. Treatment, Complications, and Clinical Outcome of 416 Patients With COVID-19

Characteristic	Patients, No. (%)			P value
	All (n = 416)	Cardiac injury With (n = 82)	Without (n = 334)	
Time from symptom onset to admission, median (range), d	10 (1-30)	10 (1-30)	10 (1-28)	.27
Treatment				
Oxygen inhalation	316 (76.0)	26 (31.7)	290 (86.8)	<.001
Noninvasive ventilation	51 (12.3)	38 (46.3)	13 (3.9)	<.001
Invasive mechanical ventilation	32 (7.7)	18 (22.0)	14 (4.2)	<.001
Continuous renal replacement therapy	2 (0.5)	2 (2.4)	0	.04
Antiviral treatment	403 (96.9)	82 (100)	321 (96.1)	.08
Glucocorticoids	304 (73.1)	72 (87.8)	232 (69.5)	<.001
Intravenous immunoglobulin therapy	259 (62.3)	68 (82.9)	191 (57.2)	<.001
Antibiotic treatment	235 (56.5)	68 (82.9)	167 (50)	<.001
Complications				
ARDS	97 (23.3)	48 (58.5)	49 (14.7)	<.001
Acute kidney injury	8 (1.9)	7 (8.5)	1 (0.3)	<.001
Electrolyte disturbance	30 (7.2)	13 (15.9)	17 (5.1)	.003
Hypoproteinemia	27 (6.5)	11 (13.4)	16 (4.8)	.01
Anemia	13 (3.1)	4 (4.9)	9 (2.7)	.30
Coagulation disorders	12 (2.9)	6 (7.3)	6 (1.8)	.02
Clinical outcome				
Remained in hospital	319 (76.7)	38 (46.3)	281 (72.2)	<.001
Discharged	40 (9.6)	2 (2.4)	38 (23.4)	
Died	57 (13.7)	42 (51.2)	15 (4.5)	<.001

Mortality in Patients with and Without Cardiac Injury

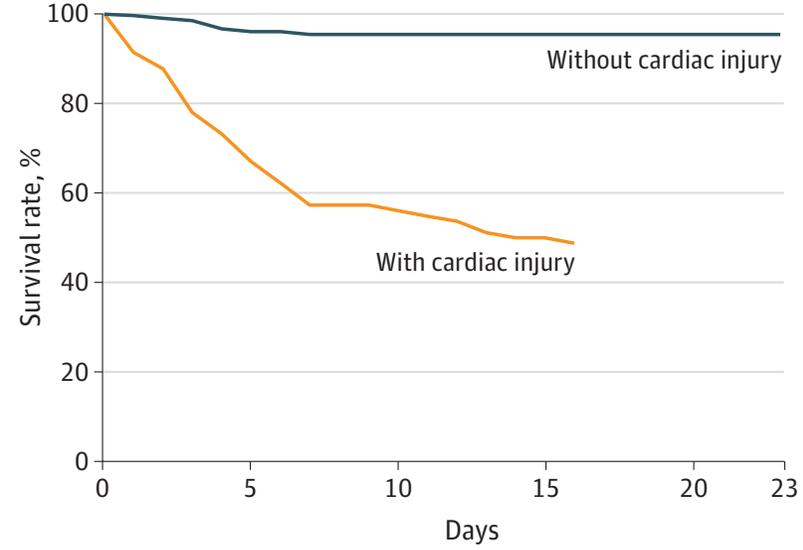
Figure 2. Mortality During Hospitalization Between Patients With vs Without Cardiac Injury

A Time from symptom onset



No. at risk	0	10	20	30	37
With cardiac injury	82	68	46	40	40
Without cardiac injury	334	329	323	320	319

B Time from admission



No. at risk	0	5	10	15	20	23
With cardiac injury	82	55	46	41	0	0
Without cardiac injury	334	321	319	319	319	319

	No. of events/ No. of patients	Time from symptom onset		Time from admission	
		Duration, mean (range), d	<i>P</i> value log-rank	Duration, mean (range), d	<i>P</i> value log-rank
With cardiac injury	42/82	15.6 (1-37)	<.001	6.3 (1-16)	<.001
Without cardiac injury	15/334	16.9 (3-37)		7.8 (1-23)	

Risk Factor Associated with Mortality

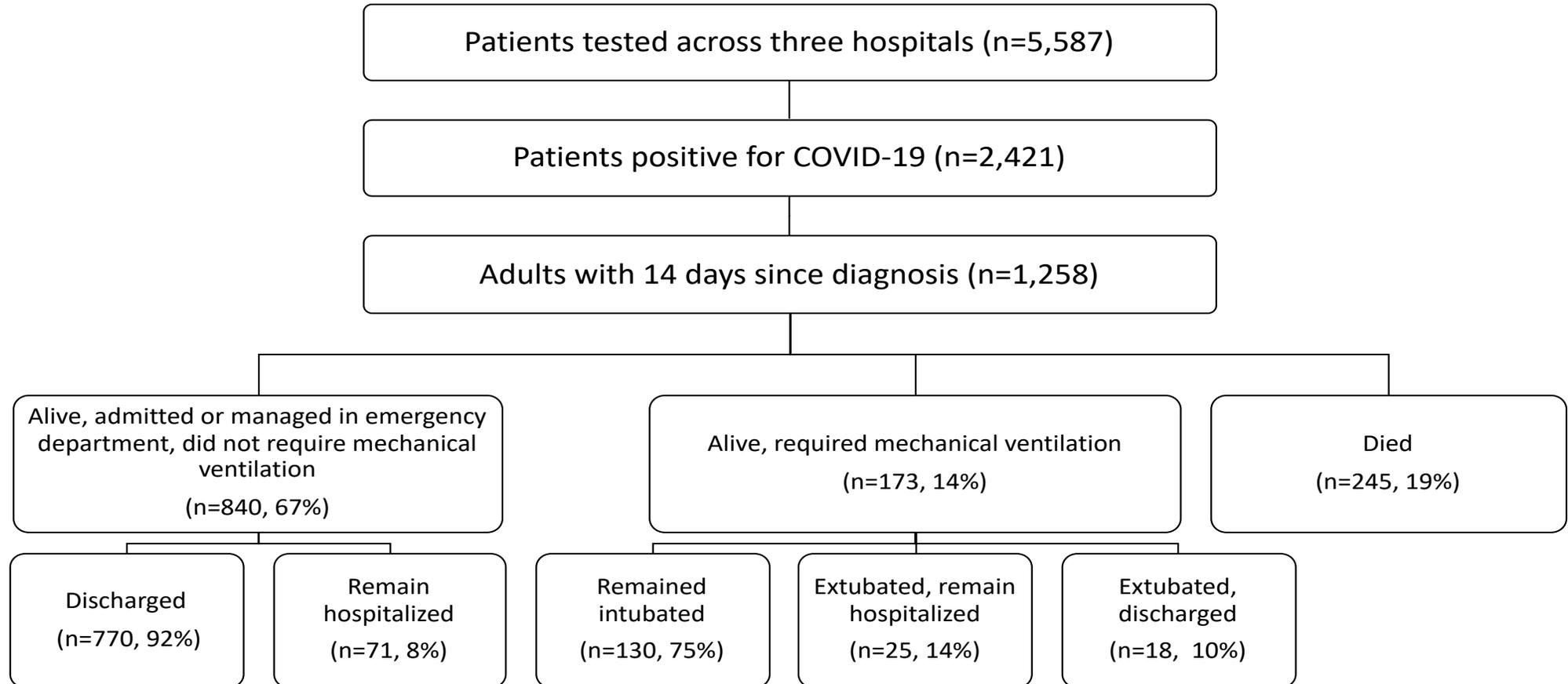
Table 3. Multivariate Cox Regression Analysis on the Risk Factors Associated With Mortality in Patients With COVID-19

Factor	From symptom onset		From admission	
	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Age, y	1.02 (0.99-1.05)	.07	1.02 (0.99-1.04)	.18
Cardiovascular diseases	1.51 (0.70-3.30)	.30	1.40 (0.65-3.03)	.39
Cerebrovascular diseases	1.12 (0.46-2.70)	.80	1.71 (0.71-4.09)	.25
Diabetes	0.79 (0.41-1.52)	.48	0.75 (0.38-1.50)	.42
Chronic obstructive pulmonary disease	0.37 (0.04-3.50)	.38	0.39 (0.04-3.68)	.41
Renal failure	1.10 (0.49-2.44)	.82	0.66 (0.29-1.46)	.30
Cancer	1.75 (0.43-7.16)	.44	0.82 (0.18-3.65)	.79
Acute respiratory distress syndrome	7.89 (3.73-16.66)	<.001	7.11 (3.31-15.25)	<.001
Cardiac injury	4.26 (1.92-9.49)	<.001	3.41 (1.62-7.16)	.001
Creatinine \geq 1.50 mg/dL	0.59 (0.29-1.23)	.16	1.22 (0.60-2.50)	.58
N-terminal pro-B-type natriuretic peptide \geq 900 pg/mL	1.16 (0.54-2.47)	.70	1.52 (0.74-3.10)	.25

CUMC CACC COVID 19 Study

- We analyzed patients with moderate-severe COVID-19 diagnosed between March 1 – April 3, 2020 at a tertiary medical center in New York City.
- Demographics, comorbidities, symptoms, and laboratory testing were abstracted including cardiac enzymes.
- Data was captured from electronic medical record through automated abstraction or manual chart review.
- Electrocardiograms (ECGs) completed within 24 hours from presentation were read by electrophysiologists to assess for abnormalities (any abnormality of rate, rhythm, intervals or wave forms other than sinus tachycardia or 1st degree heart block).
- Clinical outcomes were assessed with a minimum of 14 days of follow-up.

Patient Outcomes at CUMC Sphere



Baseline Characteristics

	Worst Outcome by Fourteen Days from Diagnosis			
	Total (%)	Admitted ^a (%)	Alive, required mechanical ventilation (%)	Died (%)
	1258	840	173	245
Demographics				
Age, mean (SD)	61.6 (18.4)	58.1 (17.7)	58.3 (14.6)	76 (13.8)
Male sex	695 (55)	435 (52)	109 (63)	151 (62)
Comorbidities				
No comorbidities	209 (17)	174 (21)	27 (16)	8 (3)
Hypertension	699 (56)	426 (51)	95 (55)	178 (73)
Diabetes	445 (35)	272 (32)	63 (36)	110 (45)
Obesity	421 (33)	282 (34)	74 (43)	65 (27)
Asthma or COPD	204 (16)	138 (16)	25 (14)	41 (17)
CKD	194 (15)	106 (13)	18 (10)	70 (29)
HFrEF	80 (6)	47 (6)	6 (3)	27 (11)
HFpEF	52 (4)	31 (4)	4 (2)	17 (7)
CAD	140 (11)	83 (10)	10 (6)	47 (19)
Cancer, active	51 (4)	34 (4)	6 (3)	11 (4)
Cancer, history	70 (6)	43 (5)	10 (6)	17 (7)
Two or more comorbidities	696 (55)	437 (52)	92 (53)	167 (68)

Presentation Symptoms and Vital Signs

	Worst Outcome by Fourteen Days from Diagnosis			
	Total (%)	Admitted ^a (%)	Alive, required mechanical ventilation (%)	Died (%)
	1258	840	173	245
Presenting Symptoms				
Fever	491 (39)	334 (40)	71 (41)	86 (35)
Cough	404 (32)	288 (34)	57 (33)	59 (24)
Shortness of breath	370 (29)	224 (27)	70 (40)	76 (31)
Gastrointestinal complaints	113 (9)	95 (11)	12 (7)	6 (2)
Weakness	84 (7)	58 (7)	10 (6)	16 (7)
Chest pain	40 (3)	32 (4)	7 (4)	1 (0)
Altered mental status	38 (3)	13 (2)	6 (3)	19 (8)
Presenting Vital Signs				
Abnormal Temperature (>101.4 or <96.6 F)	361 (29)	231 (28)	60 (35)	70 (29)
Abnormal Heart Rate (>100 or <60 bpm)	558 (44)	363 (43)	89 (51)	106 (43)
Abnormal oxygen saturation (< 96%)	719 (57)	439 (52)	136 (79)	144 (59)
Respiratory rate ≥20	624 (50)	366 (44)	108 (62)	150 (61)
Systolic blood pressure < 100 mmHg	110 (9)	71 (8)	13 (8)	26 (11)

ECG Finding

	Worst Outcome by Fourteen Days from Diagnosis			
	Total (%)	Admitted ^a (%)	Alive, required mechanical ventilation (%)	Died (%)
	1258	840	173	245
Presenting Electrocardiogram				
Normal ECG	204 (16)	152 (18)	33 (24)	19 (10)
Borderline ECG	121 (10)	87 (10)	19 (14)	15 (8)
Abnormal ECG	562 (45)	325 (39)	86 (62)	151 (82)

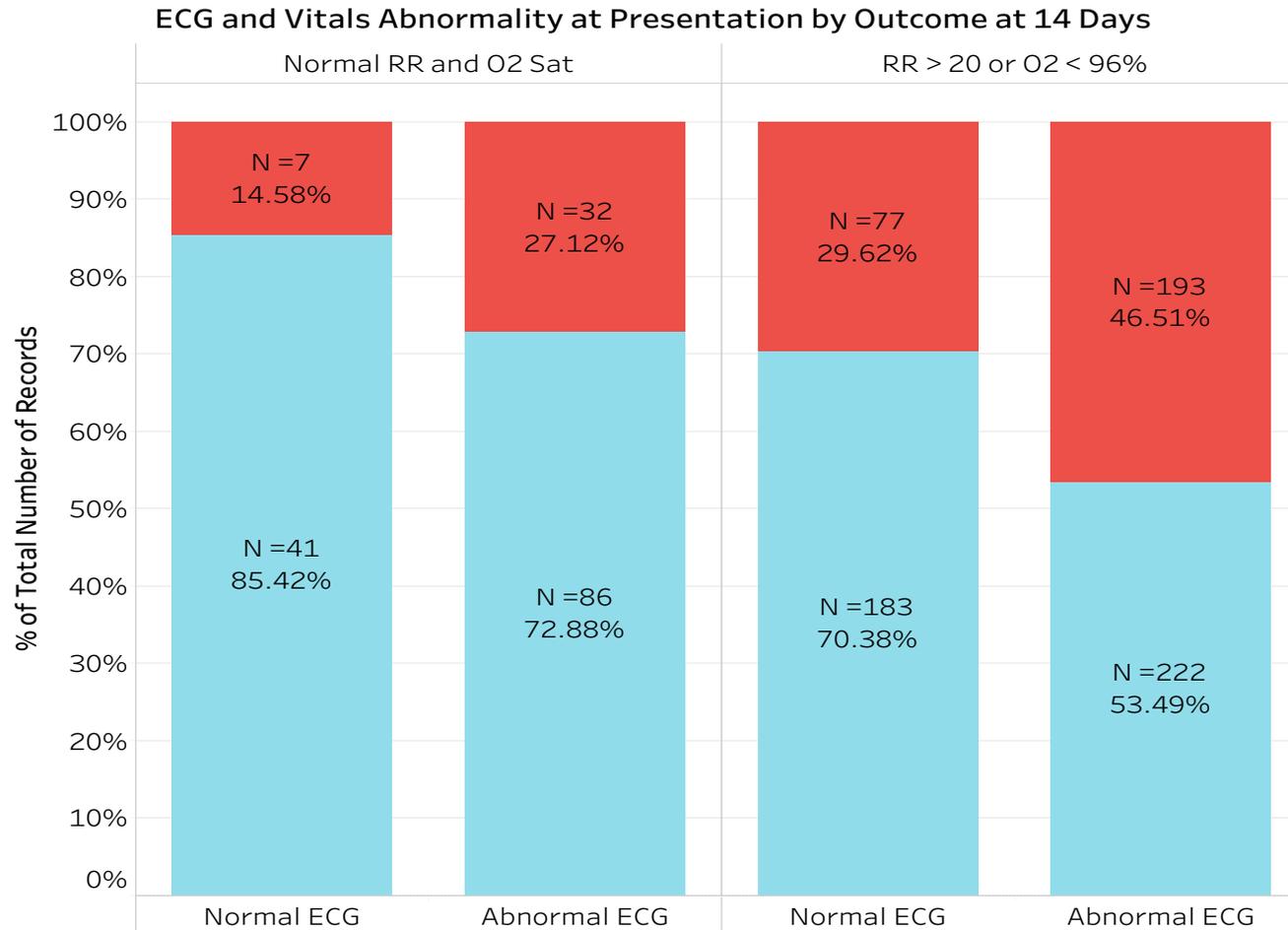
ECG Finding

		Total		Admitted or managed in ED			Required mechanical ventilation		Died	
Total		887		564	100%		138	100%	185	100%
Rhythm										
	Normal sinus rhythm	583	66%	395	70%		88	64%	100	54%
	Sinus bradycardia	15	2%	13	2%		0	0%	2	1%
	Sinus tachycardia	225	25%	132	23%		44	32%	49	26%
	Atrial fibrillation or atrial flutter	46	5%	15	3%		6	4%	25	14%
	Paced rhythm	12	1%	6	1%		0	0%	6	3%
	Other	6	1%	3	1%		0	0%	3	2%
ECG intervals, median		Median		Median			Median		Median	
	Ventricular rate (bpm)	90		88			95		94	
	PR interval, ms	150		150			146		150	
	QRS interval, ms	86		86			86		88	
	QT, ms	364		370			358		360	
	QTc (Bazett), ms	445		443			443		452	
	QTc (Fridericia), ms	416		415			410		422	

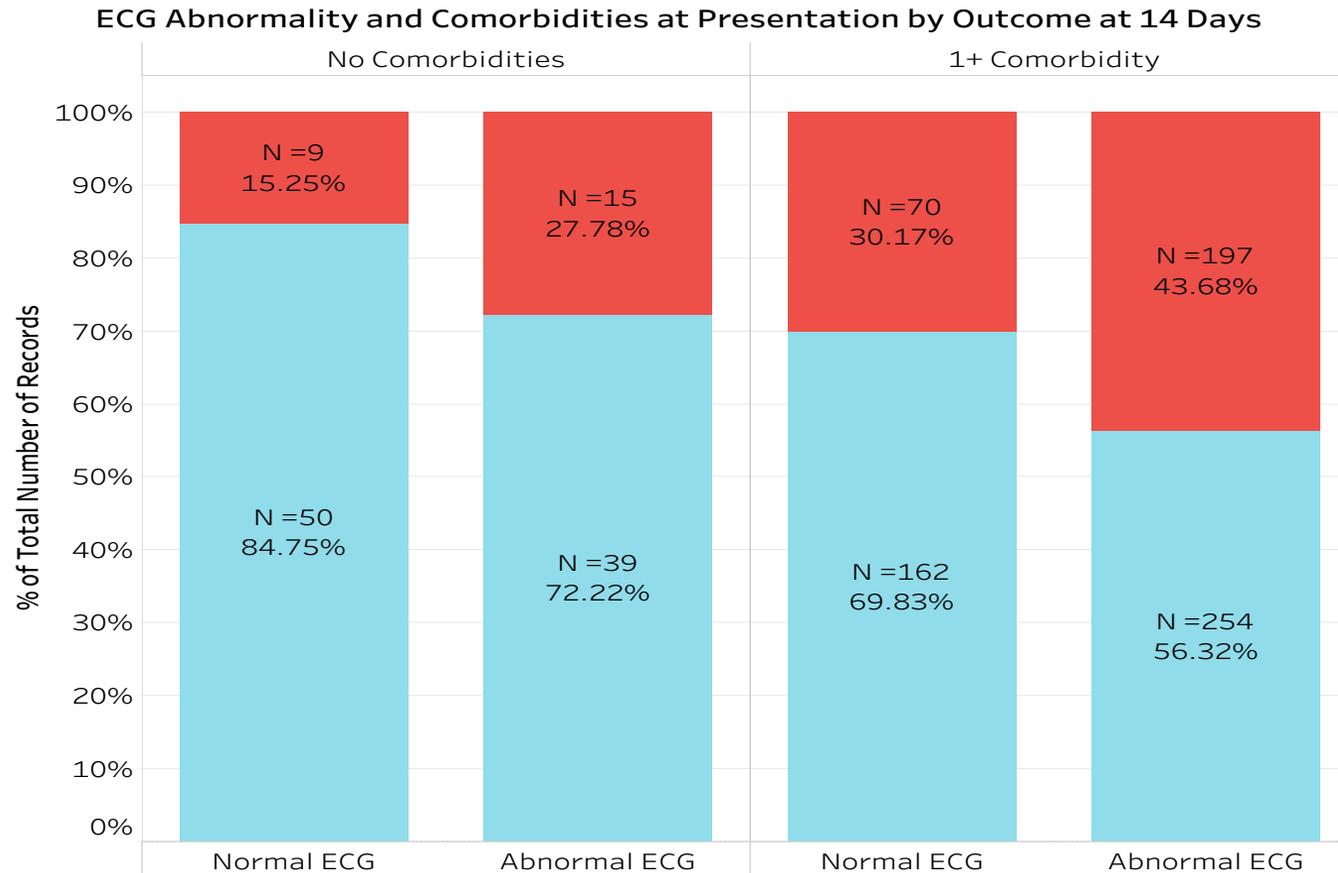
		Total		Admitted or managed in ED			Required mechanical ventilation		Died	
Pathologic Q waves		71	8%	41	7%		5	4%	25	14%
ST and T wave analyses restricted to QRS <120		812		531			129		152	
	Normal ST and TW	506	62%	348	66%		76	59%	82	54%
	Abnormal ST or TW	306	38%	183	34%		53	41%	70	46%
	Significant ST depression	31	4%	16	3%		7	5%	8	5%
	Significant ST elevation	11	1%	5	1%		4	3%	2	1%
	Significant ST depression or elevation	42	5%	21	4%		11	9%	10	7%
Any atrial ectopic beat		67	8%	35	6%		3	2%	29	16%
Any ventricular ectopic beat		48	5%	24	4%		2	1%	22	12%
QTc (Bazett)	QRS <120, QTc <460	603	74%	399	71%		102	74%	102	55%
	QRS <120, QTc >=460 and <500	172	21%	116	21%		22	16%	34	18%
	QRS <120, QTc >500	37	5%	16	3%		5	4%	16	9%
	QRS >=120, QTc <500	44	59%	19	3%		7	5%	18	10%
	QRS >=120, QTc >=500, <550	25	33%	13	2%		2	1%	10	5%
	QRS >=120, QTc >=550	6	8%	1	0%		0	0%	5	3%
QRS voltage	LVH	99	11%	53	9%		14	10%	32	17%
	Low voltage	30	3%	19	3%		3	2%	8	4%

rs

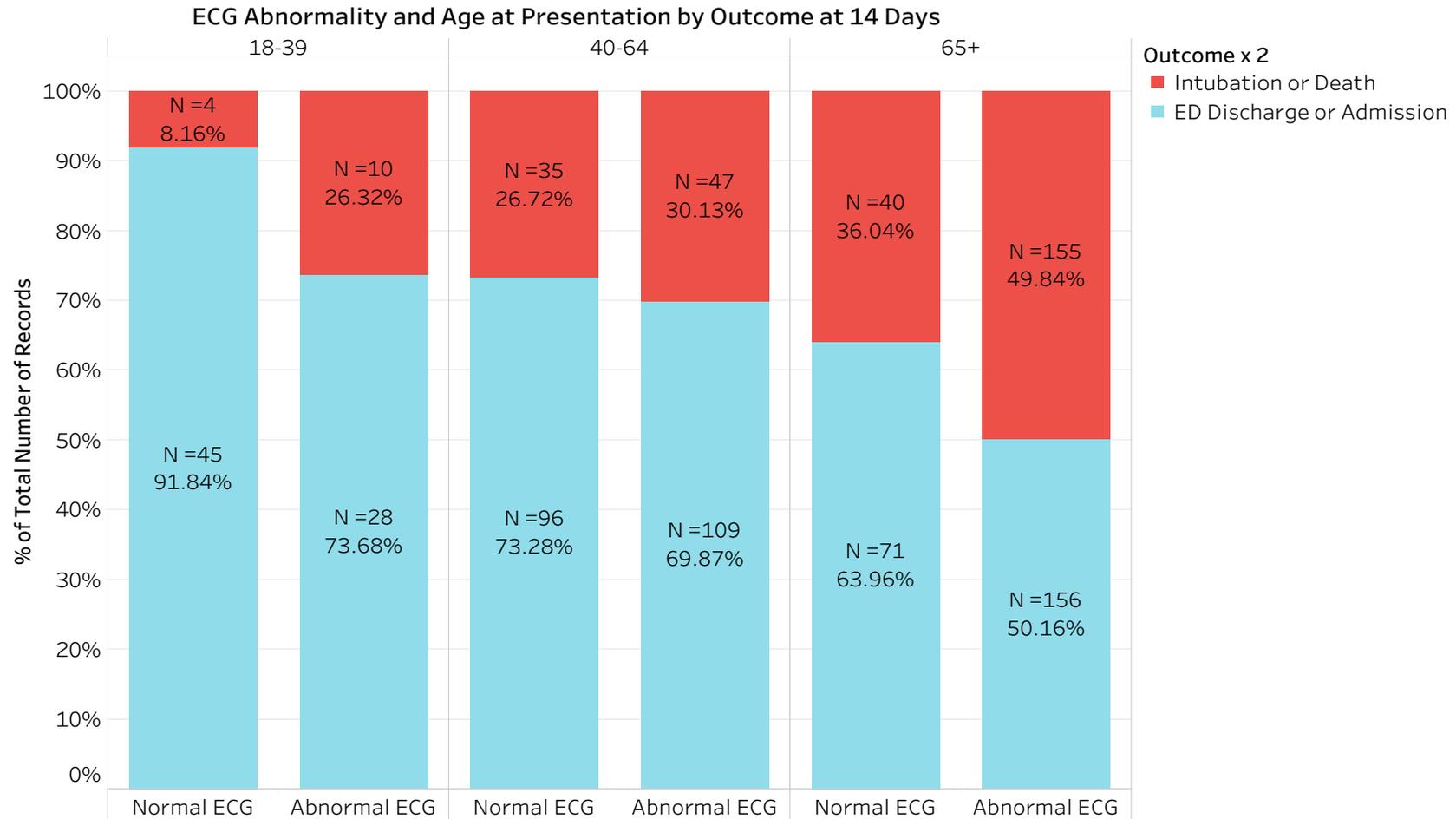
EKG abnormalities at time of presentation is prognostic of intubation or death at 14 days – Vital signs



EKG abnormalities at time of presentation is prognostic of intubation or death at 14 days – Comorbidities



EKG abnormalities at time of presentation is prognostic of intubation or death at 14 days – Age



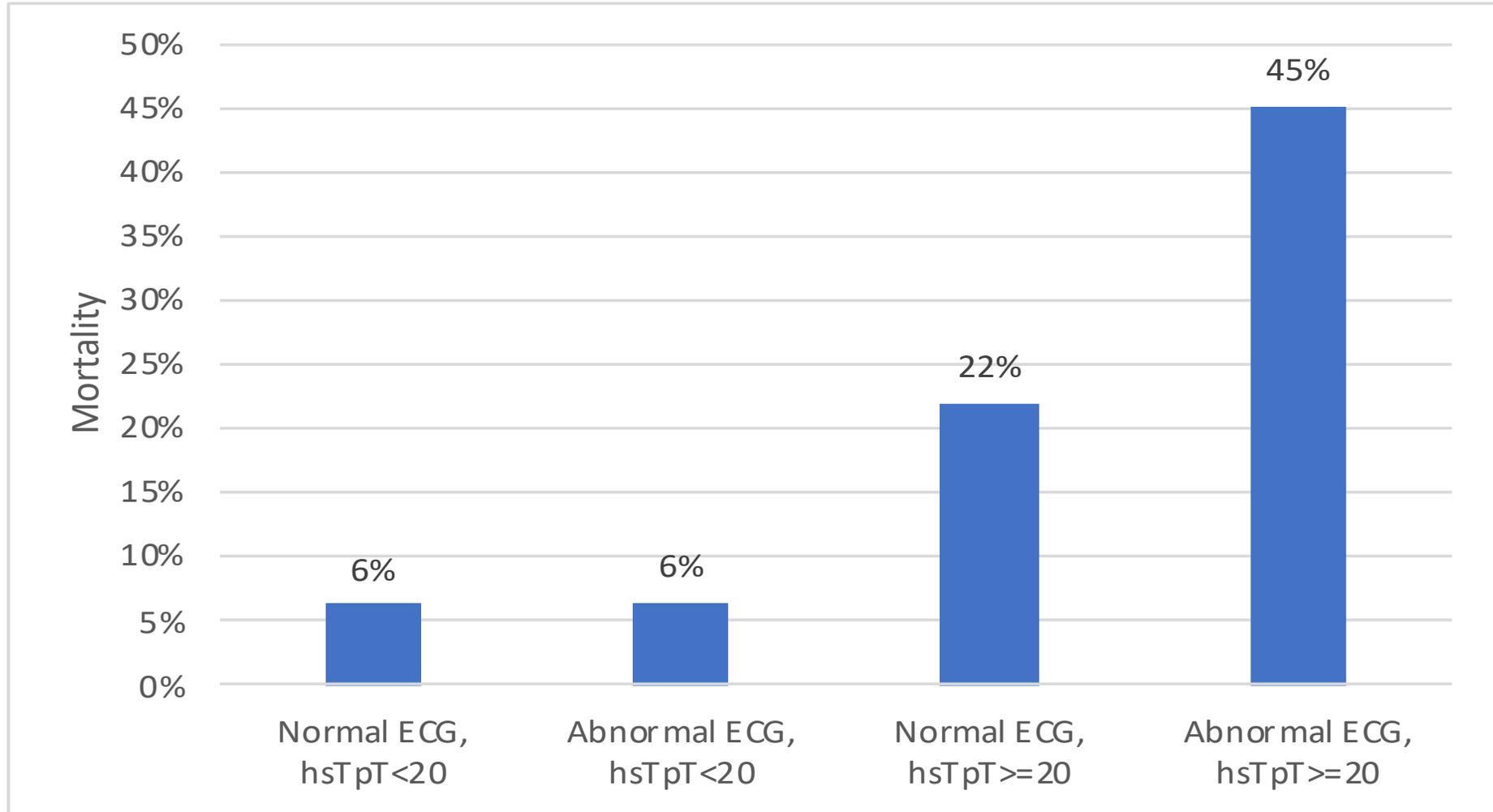
Lab Results

		Total	Did not require hospitalization	Required Hospitalization	Required Mechanical Ventilation	Died	p value (death/ventilated vs. favorable outcome)
Creatinine	Presenting	1.8	0.8	1.6	1.8	2.3	0.000
	Peak	2.7	0.8	1.9	4.6	3.8	0.000
BUN	Presenting	24.7	11.4	20.8	26.5	37.4	0.000
	Peak	42.0	13.0	27.7	77.8	65.9	0.000
NT-proBNP	Presenting	4890.6	225.7	3545.1	3308.3	9203.2	0.008
	Peak	4964.9	225.7	3550.8	3715.6	9216.6	0.010
hsTpT	Presenting	55.1	10.3	28.0	60.6	135.1	0.000
	Peak	117.6	10.3	33.7	220.0	299.9	0.000
D-dimer	Presenting	3.0	0.8	2.1	4.4	4.9	0.000
	Peak	5.5	0.9	2.7	13.4	8.5	0.000
LDH	Presenting	449.7	802.6	373.9	583.4	571.7	0.000
	Peak	589.2	802.6	416.7	866.1	913.6	0.000

Lab Results

		Total	Did not require hospitalization	Required Hospitalization	Required Mechanical Ventilation	Died	p value (death/ventilated vs. favorable outcome)
CRP	Presenting	122.0	87.3	99.8	163.4	163.1	0.000
	Peak	165.6	90.4	124.4	271.3	220.1	0.000
Procalcitonin	Presenting	1.9	0.1	0.8	4.1	3.9	0.000
	Peak	7.4	0.2	1.3	16.4	20.2	0.000
Sedimentation rate	Presenting	67.5	50.1	65.4	73.8	70.0	0.004
	Peak	84.0	52.0	76.1	110.2	90.1	0.000
Interleukin-6	Presenting	131.3	15.4	71.9	187.1	189.5	0.000
	Peak	101.7	15.4	43.6	238.0	177.0	0.000
WBC	Presenting	8.2	7.2	7.3	11.1	9.4	0.000
	Peak	12.5	9.1	9.3	22.6	16.3	0.000

Mortality by ECG Categorization and High Sensitivity Troponin



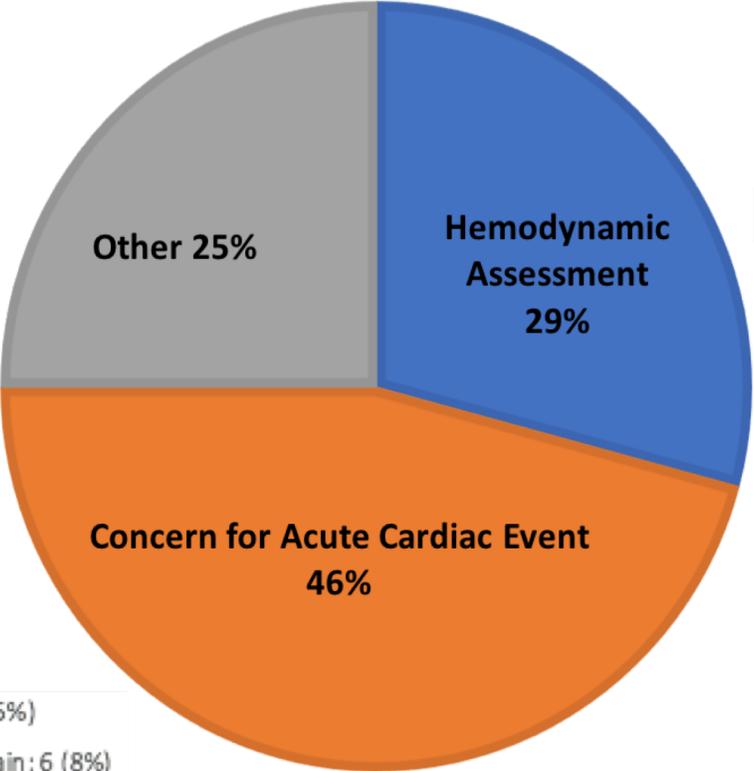
Indications for Performing a Transthoracic Echocardiogram

Other: 18

- Other: 3 (4%)
- Cardiac History: 4 (6%)
- Vegetation: 3 (4%)
- Arryhtmia: 4 (6%)
- Stroke Evaluation: 4 (6%)

Concern for Acute Cardiac Event: 33

- Elevated Cardiac Biomarkers: 11 (15%)
- Acute Coronary Syndrome/Chest Pain: 6 (8%)
- Heart Failure/Myocarditis: 8 (11%)
- Pulmonary Embolism: 8 (11%)



Hemodynamic Assessment: 21

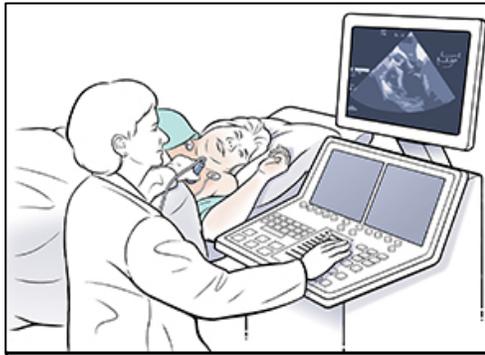
- Hemodynamic Assessment: 21 (29%)

Suspected cardiac events

Changes in ECG

Elevated biomarkers (TPI and pro-BNP)

Risk factors and symptoms



Hemodynamics instability

Cardiogenic shock

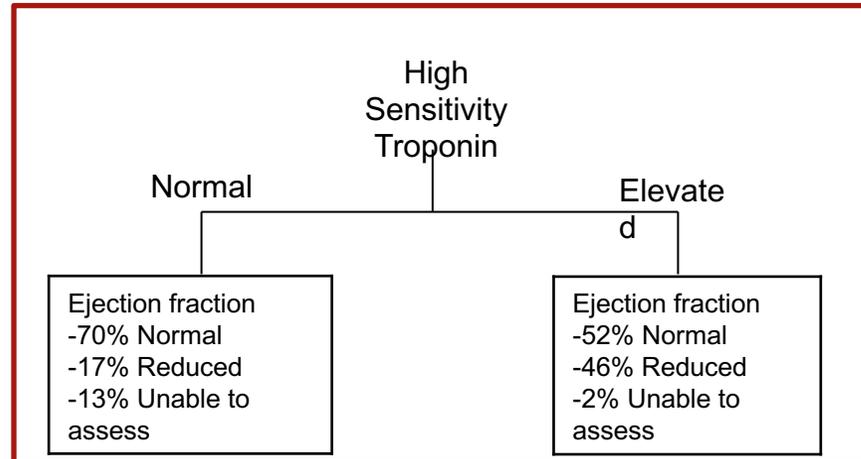
Mix shock

Neurogenic shock

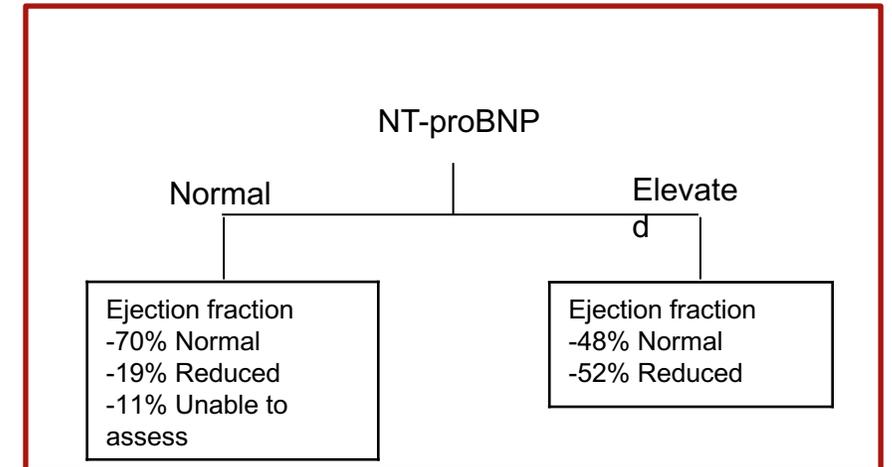
Study Characteristics

- 72 echocardiograms performed
- Average study: 39.7 clips, 6.7 minutes
- Study quality:
 - 40% adequate or mildly limited
 - 40% moderately limited

Left Ventricle



Left Ventricle



Right Ventricle

Size

-69% Normal

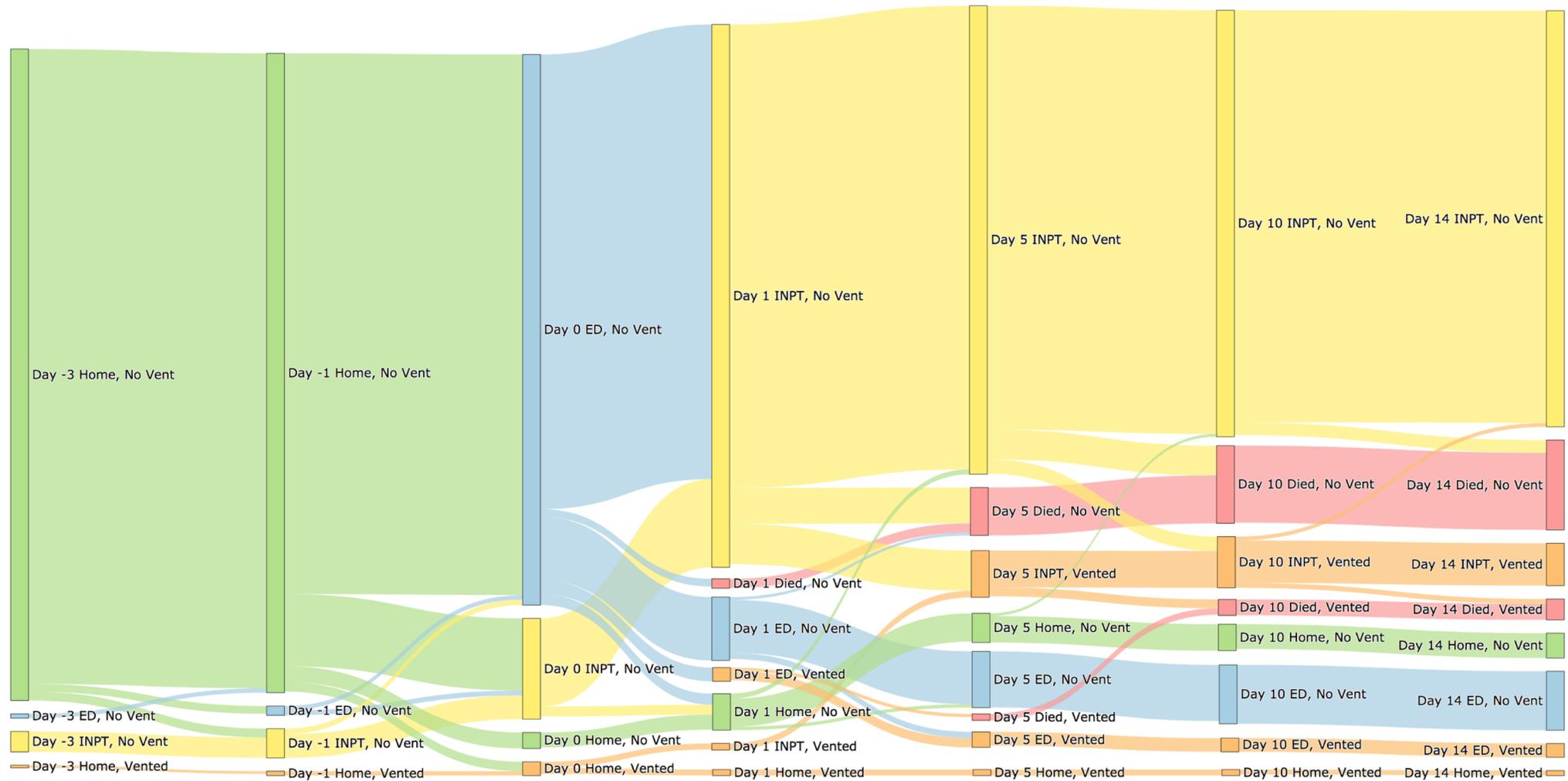
-31% Abnormal

Function

-47% Normal

-53% Abnormal

Patient Course Following Admission



Main Findings

- 33% of patients either died or required mechanical ventilation, and 19% of the patients died and within fourteen days of COVID-19 diagnosis
- Respiratory rate > 20/min or oxygen saturation <96% at presentation are predictive of death or need for mechanical ventilation
- Abnormal ECG was present in 63% of the patients
- The addition of an abnormal ECG to abnormal respiratory vital signs identifies a group of patients with particularly poor outcomes

Next Steps

- What is the long term effect of COVID 19 infection on the heart?
- Development of clinical cardiomyopathy as assessed by
 - ECG
 - ECHO
 - MRI
 - Functional capacity (exercise performance)
 - Metabolic changes and substrate utilization (GLU, FFA)