Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Clinical Research

The Utility of Handheld Cardiac and Lung Ultrasound in Predicting Outcomes of Hospitalised Patients With COVID-19

Ziv Dadon, MD,[a,‡] Nir Levi, MD,[a,‡] Amir Orlev, MD,[a] Daniel Belman, MD,[b] Evan Avraham Alpert, MD,[c,d] Michael Glikson, MD,[a,d] Shmuel Gottlieb, MD,[a,e,§] and Adi Butnaru, MD[a,§]

[a] *Jesselson Integrated Heart Center, Shaare Zedek Medical Center, Jerusalem, Israel*

[b] *Intensive Care Unit, Shaare Zedek Medical Center, Jerusalem, Israel*

[c] *Emergency Department, Shaare Zedek Medical Center, Jerusalem, Israel*

[d] *Faculty of Medicine Hebrew University, Jerusalem, Israel*

[e] *Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*

ABSTRACT

Background: Strict isolation precautions limit formal echocardiography use in the setting of COVID-19 infection. Information on the importance of handheld focused ultrasound for cardiac evaluation in these patients is scarce. This study investigated the utility of a handheld echocardiography device in hospitalised patients with COVID-19 in diagnosing cardiac pathologies and predicting the composite end point of in-hospital death, mechanical ventilation, shock, and acute decompensated heart failure.

RÉSUMÉ

Contexte : Les précautions d'isolement strictes limitent l'utilisation de l'échocardiographie formelle en présence de COVID-19. Les renseignements sur l'importance des appareils portatifs d'échographie focalisée pour l'évaluation cardiaque en pareil cas sont rares. La présente étude vise à examiner l'utilité d'un appareil d'échocardiographie portatif chez les patients hospitalisés atteints de COVID-19 pour le diagnostic de maladies cardiaques et pour la mesure du critère d'évaluation composé regroupant le décès en milieu

COVID-19 interacts with the cardiovascular system on multiple levels. It is well established that known cardiovascular disease or risk factors are associated with a significant increase in morbidity and mortality among patients with COVID-19. In addition, it has been demonstrated that elevation in cardiac biomarkers such as high-sensitivity cardiac troponin I (hs-cTnI) is correlated with a poor prognosis in COVID-19 patients.[1]

The association between COVID-19 and the cardiovascular system has led researchers to try to better identify predictors for severe disease and adverse outcomes. Possible predictors for disease severity might be cardiac systolic function, including left (LV) and right (RV) ventricular systolic function or valvular functional abnormalities as determined with the use of echocardiography. Routine echocardiographic evaluation of all patients admitted with COVID-19, however, is currently discouraged according to various guidelines and consensus papers owing to concerns of excessive workload in the setting of a pandemic,[2,3] risk of infection of echocardiography professionals, and increased equipment contamination with long imaging times.[4]

Handheld ultrasound has been shown to be accurate when used by cardiologists for many aspects of cardiac evaluation. This includes evaluation of LV ejection fraction (LVEF), regional wall motion abnormalities, LV hypertrophy, inferior vena cava size, valvular pathology, and pericardial effusion.[5,6] As point-of-care ultrasound (POCUS) is increasingly being used, its application in cardiac systolic function assessment is likely to markedly increase.[7,8] LVEF, RV systolic function, and basic valvular function can be determined on admission by means of bedside echocardiography using the POCUS approach.[9,10] In addition, echocardiography with the use of handheld devices can be performed by noncardiologists, does

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‡Drs Dadon and Levi contributed equally to this work.

§Drs Gottlieb and Butnaru contributed equally to this work.

Corresponding author: Dr Shmuel Gottlieb, Jesselson Integrated Heart Center, Shaare Zedek Medical Center, Shmu'el-Bait St 12, Jerusalem, 9103102, Israel. Tel.: +972-26555975.

E-mail: shmuelg@ekmd.huji.ac.il

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Methods: From April 28 through July 27, 2020, consecutive patients diagnosed with COVID-19 underwent evaluation with the use of handheld ultrasound (Vscan Extend with Dual Probe; GE Healthcare) within 48 hours of admission. The patients were divided into 2 groups: "normal" and "abnormal" echocardiogram, as defined by biventricular systolic dysfunction/enlargement or moderate/severe valvular regurgitation/stenosis.

Results: Among 102 patients, 26 (25.5%) had abnormal echocardiograms. They were older with more comorbidities and more severe presenting symptoms compared with the group with normal echocardiograms. The prevalences of the composite outcome among low- and high-risk patients (oxygen saturation $<$ 94%) were 3.1% and 27.1%, respectively. Multivariate logistic regression analysis revealed that an abnormal echocardiogram at presentation was independently associated with the composite end point (odds ratio 6.19, 95% confidence interval 1.50-25.57; $P = 0.012$).

Conclusions: An abnormal echocardiogram in COVID-19 infection settings is associated with a higher burden of medical comorbidities and independently predicts major adverse end points. Handheld focused echocardiography can be used as an important "rule-out" tool among high-risk patients with COVID-19 and should be integrated into their routine admission evaluation. However, its routine use among low-risk patients is not recommended.

Méthodologie : Du 28 avril au 27 juillet 2020, des patients consécutifs ayant reçu un diagnostic de COVID-19 ont été évalués au moyen d'un échographe portatif (échographe Vscan Extend à double sonde de GE Healthcare) dans les 48 heures suivant leur admission. Les patients ont été répartis en deux groupes selon que l'échocardiogramme était « normal » ou « anormal », l'évaluation étant fondée sur la présence d'une dysfonction systolique ou d'une hypertrophie biventriculaire, ou d'une régurgitation ou d'une sténose valvulaires modérées ou graves.

Résultats : Parmi les 102 patients, 26 (25,5 %) présentaient un échocardiogramme anormal. Ils étaient plus âgés, avaient plus des comorbidités et présentaient des symptômes plus graves comparativement aux patients dont l'échocardiogramme était normal. La prévalence des manifestations formant le critère d'évaluation composé, chez les patients à risque faible et les patients à risque élevé (saturation en oxygène $<$ 94 %), a été de 3,1 % et de 27,1 %, respectivement. Une analyse de régression logistique multivariée a révélé qu'un échocardiogramme anormal lors de l'admission était associé de façon indépendante au critère d'évaluation composé (rapport de cotes : 6,19, intervalle de confiance à 95 % : 1,50-25,57; $p = 0,012$).

Conclusions : Un échocardiogramme anormal dans un cas de COVID-19 est associé à un fardeau plus lourd sur le plan des maladies concomitantes, et permet de prédire de façon indépendante la survenue de manifestations graves. L'échocardiographie focalisée réalisée à l'aide d'un appareil portatif peut être un outil important pour exclure certains troubles chez les patients à risque élevé atteints de COVID-19 et devrait être intégrée dans l'évaluation systématique de ces patients au moment de l'admission. Toutefois, son utilisation systématique chez les patients à risque faible n'est pas recommandée.

not need a sonography technician, can be easily cleaned, and can be stored in COVID-19 units for ease of use without disruption to the clinical setting. Furthermore, some devices can be used for lung assessment as well, with a quick and $>$ 90% accurate interpretation for common causes of acute respiratory failure.[11]

The objective of the present study was to characterise the utility of handheld echocardiography in hospitalised patients with COVID-19 to predict end points based on identified cardiac abnormalities, including ventricular size and systolic function, and valvular pathologies.

Methods

Study setting

This was a prospective study of real-time focused echocardiography and lung ultrasound performed using a handheld device. The study was conducted on consecutive patients with polymerase chain reaction—confirmed COVID-19 hospitalised in designated medical wards at a tertiary care medical center from April 28 through July 27, 2020. The study was approved by the hospital's institutional review board.

All echocardiographic clips were acquired by cardiologists or intensivists and were later interpreted by a fellowship-trained echocardiographer. Variables including demographics, past medical history, electrocardiography (ECG), imaging modalities, and laboratory results obtained from the medical record.

Study end points

The primary end point was defined as a composite end point of in-hospital death, mechanical ventilation, shock, and acute decompensated heart failure (ADHF). Secondary end points included the composite end point, individual parameters of the composite end point, advanced ventilatory support (high-flow nasal cannula, noninvasive positive airway pressure support, and invasive ventilation), chronic ventilation, myocardial injury (defined as hs-cTnI $>$ 3 times upper normal limit), venous thromboembolism, anti—COVID-19 drug use, sepsis, and length of hospital stay.

Study protocol

Patients with confirmed COVID-19 who were hospitalised in designated internal medicine departments were recruited into the study. Conscious patients consented verbally. Patients who were not able to give informed consent underwent echocardiography if it was clinically indicated. Patients that refused to participate in the study were excluded. Basic characteristics included age, sex, and known previous medical illness. Routine chest X-ray, ECG, and blood workup were performed for every patient on admission to the designated COVID-19 wards. The routine laboratory tests included complete blood count, renal function, electrolytes, hs-cTnI, D-dimer, coagulation function tests, and C-reactive protein (CRP). B-Type natriuretic peptide was measured according to

the clinical judgment of the treating physician. The study physicians performing the ultrasound examination wore personal protective equipment including a full gown, N95 face mask, face shield, and at least 2 sets of gloves. Participants were evaluated by focused echocardiographic examination and lung ultrasound within 48 hours of their hospitalisation with the use of a handheld ultrasound machine (Vscan Extend with Dual Probe; General Electric, Northville, MI). The cardiac POCUS was conducted using the sector transducer from the apical, parasternal, and substernal views. Valves were evaluated visually using both 2-dimensional (2D) and color Doppler echocardiography. The acquired video clips were stored in the Digital Imaging and Communications in Medicine format and sent wirelessly to a picture archiving and use platform (McKesson Cardiology, version 14.0, Alpharetta, GA, USA) routinely used by the cardiology department. The echocardiogram clips were then interpreted by visual evaluation by an experienced echocardiographer (A.B.), blinded to the patient's clinical course and presentation, for evaluation of LVEF and LV diameter, RV visual systolic function and RV diameter, severity of valvular dysfunction (the valves were visually assessed for functional abnormalities, ie, regurgitation or stenosis, with the use of both 2D and Doppler echocardiograms), pericardial effusion, and any additional significant echocardiographic findings. Offline measurements of LV end-diastolic diameter (LVEDD), tricuspid annular plane systolic excursion (TAPSE), and fractional area change were made. POCUS lung ultrasound was performed using the linear transducer and included a 10-location assessment (standard approach: 4 quadrants on each anterior hemithorax and 2 on each posterior hemithorax) for B-lines, subpleural consolidations/lung hepatisation, and pleural effusions. Each assessed variable was graded separately for each location according to the severity as 0 (normal), 1 (several lines or small consolidation/effusion), or 2 (coalescent B-lines or diffuse/widespread consolidation/effusion). The lung ultrasound assessment scoring was calculated as the sum of the entire graded variables (range of 0-20).

Data management

All data obtained in this study were entered into 2 Microsoft Excel spreadsheets. One file contained the case-identifying number, patient identifiers, and other pertinent variables. POCUS results were inserted into a second file by the patient's identifying number. The 2 files were then matched.

Study participants were divided into normal or abnormal echocardiograms according to POCUS results. Abnormal echocardiograms included those with LVEF $<$ 50%, LV dilation, RV systolic dysfunction/dilation, and moderate/severe valvular dysfunction (functional regurgitation or stenosis).

Statistical analyses

The patients were divided into normal and abnormal echocardiograms, and analyses were performed accordingly. Descriptive statistics were used to analyse differences in baseline and clinical characteristics, echocardiography and lung ultrasound results, and end points, with the use of chi-square or Fisher exact test for categoric variables and *t* test or Mann-Whitney *U* test for continuous variables, as appropriate. Test selection was based on data distribution and normalcy.

High-risk patients were defined as those with room-air oxygen saturation $<$ 94%. The ability of the echocardiography results to identify patients with and without the composite outcome was then tested for sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) among low- and high-risk patients.

Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to test the univariate associations between abnormal echocardiogram and the composite end point and individual end points.

Multivariate logistic regression analysis (OR and 95% CI) was calculated for the association between abnormal echocardiogram and the composite end point among the entire cohort and individually among high-risk patients, including pertinent baseline characteristics covariates (those with *P* values $<$ 0.05). Statistical analyses were performed with the use of SPSS Statistics for Windows version 21 (SPSS, Chicago, IL, USA).

Results

A total of 102 hospitalised patients with COVID-19 were recruited into the study, including 76 (74.5%) with normal and 26 (25.5%) with abnormal echocardiograms (Table 1). Four patients refused to participate in the trial and were therefore excluded.

Baseline and medical characteristics

As presented in Table 1, the mean age of the total cohort was 59.7 $\pm$ 18.4 years, and 63.7% were male. Patients with an abnormal echocardiogram were older and more likely to suffer from comorbidities including smoking, hypertension, hyperlipidemia, ischemic heart disease, past revascularisation, and heart failure compared with patients with a normal echocardiogram. They had a higher proportion of past valve replacement and cardiac implantable electronic devices. Moreover, they were treated more often with chronic heart failure evidence-based medications, antiplatelets, diuretics, and statins.

Presentation characteristics and laboratory results

As presented in Table 1, the 2 groups did not differ in their presenting complaints or vital signs. Patients with abnormal echocardiograms had a higher rate of pathologic ECG (including nonspecific and ST-segment changes or T-wave inversion) and chest X-ray infiltrates, compared with those with normal echocardiograms. Laboratory results of creatinine, hs-cTnI, fibrinogen, activated partial thromboplastin time, white blood cell count, neutrophil/lymphocyte count ratio, CRP, and D-dimer were higher in the abnormal than in the normal echocardiogram group, whereas albumin was lower.

Echocardiography and lung ultrasound results

Echocardiography and lung ultrasound results are presented in Table 2. Compared with patients with a normal echocardiogram, those with an abnormal echocardiogram had

Table 1. Baseline and clinical characteristics

Variable	All (n = 102)	Normal echocardiogram (n = 76)	Abnormal echocardiogram (n = 26)	*P* value
Baseline characteristics				
Age, years	59.7 ± 18.4	57.0 ± 18.6	67.6 ± 15.5	0.010
Male	65 (63.7)	48 (63.2)	17 (65.4)	0.838
Body mass index, kg/m^2	27.9 ± 6.2	27.6 ± 6.2	28.9 ± 6.2	0.378
Smoking	16 (15.7)	8 (10.5)	8 (30.8)	0.014
Diabetes mellitus	33 (32.4)	21 (27.6)	12 (46.2)	0.081
Hypertension	39 (38.2)	23 (30.3)	16 (61.5)	0.005
Hyperlipidemia	32 (31.4)	18 (23.7)	14 (53.8)	0.004
IHD	20 (19.6)	9 (11.8)	11 (42.3)	0.001
CVA	5 (4.9)	2 (2.6)	3 (11.5)	0.103
Revascularisation	17 (16.7)	7 (9.2)	10 (38.5)	0.001
Heart failure	12 (11.8)	3 (3.9)	9 (34.6)	< 0.001
Valve replacement	3 (2.9)	0 (0.0)	3 (11.5)	0.015
CIED	3 (2.9)	0 (0.0)	3 (11.5)	0.015
Cognitive decline	23 (22.5)	14 (18.4)	9 (34.6)	0.088
Debilitation	26 (25.5)	16 (21.1)	10 (38.5)	0.079
Chronic lung disease	9 (8.8)	6 (7.9)	3 (11.5)	0.690
Liver disease	2 (2.0)	2 (2.6)	0 (0.0)	1.000
Previous VTE	4 (3.9)	2 (2.6)	2 (7.7)	0.268
Malignancy	2 (2.0)	1 (1.3)	1 (3.8)	0.447
Immunosuppression	4 (3.9)	3 (3.9)	1 (3.8)	1.000
Hypothyroidism	13 (12.7)	8 (10.5)	5 (19.2)	0.251
Chronic medications				
ACE-I/ARB	24 (23.5)	14 (18.4)	10 (38.5)	0.038
β-Blockers	29 (28.4)	15 (19.7)	14 (53.8)	0.001
CCB	12 (11.8)	9 (11.8)	3 (11.5)	1.000
Antiplatelets	26 (25.5)	12 (15.8)	14 (53.8)	< 0.001
Oral anticoagulation	13 (12.7)	8 (10.5)	5 (19.2)	0.251
Diuretics	11 (10.8)	4 (5.3)	7 (26.9)	0.005
Inhalations	7 (6.9)	5 (6.6)	2 (7.7)	1.000
SGLT2 inhibitors	7 (6.9)	5 (6.6)	2 (7.7)	1.000
Statins	33 (32.4)	17 (22.4)	16 (61.5)	< 0.001
COVID-19 presentation				
Chest pain	28 (27.5)	22 (28.9)	6 (23.1)	0.563
Shortness of breath	54 (52.9)	37 (48.7)	17 (65.4)	0.141
HR, beats/min	88.8 ± 22.3	88.1 ± 19.3	90.7 ± 30.0	0.626
SBP, mm Hg	124.3 ± 20.9	123.4 ± 19.9	126.8 ± 23.7	0.461
DBP, mm Hg	74.1 ± 12.0	73.6 ± 11.2	75.6 ± 14.3	0.375
SpO_2, %	87.4 ± 11.4	87.3 ± 11.9	87.8 ± 10.3	0.752
In-hospital course				
Sinus bradycardia	2 (2.0)	2 (2.7)	0 (0.0)	1.000
ECG changes				0.040
Normal	74 (72.5)	59 (77.6)	15 (57.7)	
Nonspecific changes	19 (18.6)	12 (15.8)	7 (26.9)	
TWI/ST-segment depression	6 (5.9)	4 (5.3)	2 (7.7)	
ST-segment elevation	2 (2.0)	0 (0.0)	2 (7.7)	
Chest X-ray infiltrates	75 (73.5)	51 (67.1)	24 (92.3)	0.012
AF/AFL	11 (10.8)	7 (9.2)	4 (15.4)	0.130
Laboratory results				
WBC (p), 10^3/μL	10.4 ± 5.7	9.6 ± 5.0	12.8 ± 6.7	0.013
ANC/ALC (a)	5.9 (3.0-10.6)	5.4 (2.6-8.9)	9.0 (4.4-13.4)	0.032
Hemoglobin (a), g/dL	13.0 ± 2.3	13.1 ± 2.1	12.6 ± 2.7	0.240
Platelets (a), 10^3/μL	200.6 ± 73.6	203.0 ± 73.3	193.2 ± 75.3	0.802
Creatinine (a), mg/dL	1.0 ± 0.7	0.9 ± 0.4	1.4 ± 1.1	0.002
K (a), mmol/L	4.0 ± 0.6	3.9 ± 0.5	4.1 ± 0.7	0.168
Albumin (t), g/dL	3.0 ± 0.8	3.1 ± 0.8	2.6 ± 0.7	0.044
hs-cTnI (p), ng/L	7.0 (5.0-40.8)	5.5 (5.0-22.0)	37 (6.5-541.5)	0.001
BNP (a), pg/mL	76.5 (22.5-229.5)	59.8 (15.0-200.8)	224.5 (94.5-753.5)	0.065
CRP (p), mg/L	13.0 ± 11.8	11.2 ± 11.6	18.2 ± 10.9	0.003
d-dimer (p), ng/mL	925 (522-1188)	803 (392-1362)	1178 (878-2707)	0.014
Fibrinogen (a), mg/dL	594.9 ± 186.5	572.9 ± 187.8	660.1 ± 169.3	0.015
aPTT (p), seconds	35.0 ± 9.7	33.9 ± 9.7	38.1 ± 9.2	0.009

Values are presented as mean ± SD, n (%), or median (interquartile range).

a, admission; ACE-I, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; AFL, atrial flutter; ALC, absolute lymphocytes count; ANC, absolute neutrophils count; aPTT, activated partial thromboplastin time; ARB, angiotensin receptor blocker; BNP, B-type natriuretic peptide; CCB, calcium channel blocker; CIED, cardiovascular implantable electronic device; CRP, C-reactive protein; CVA, cerebrovascular accident; DBP, diastolic blood pressure; ECG, electrocardiography; HR, heart rate; hs-cTnI, high sensitive cardiac troponin I; IHD, ischemic heart disease; IQR, interquartile range; K, potassium; p, peak; SBP, systolic blood pressure; SGLT2, sodium-glucose transport protein 2; SpO_2, oxygen saturation; t, trough; TWI, T-wave inversion; VTE, venous thromboembolism; WBC, white blood cells.

Table 2. Echocardiography results, measurements, and lung ultrasound score for patients with and without in-hospital advanced ventilatory support

Parameter	All (n = 102)	Normal echocardiogram (n = 76)	Abnormal echocardiogram* (n = 26)	*P* value†	No advanced ventilatory support (n = 76)	Advanced ventilatory support (n = 26)	*P* value‡
LVEF, %	53.4 ± 6.8	57.2 ± 4.1	49.2 ± 8.2	< 0.001	55.8 ± 6.3	53.4 ± 6.6	0.096
LVEF < 50%	16 (15.7)	0 (0.0)	16 (61.5)	< 0.001	9 (11.8)	7 (26.9)	0.068
LVEDD, cm	4.6 ± 0.5	4.5 ± 0.5	4.8 ± 0.6	0.016	4.6 ± 0.6	4.6 ± 0.5	0.692
RV dysfunction	8 (7.8)	0 (0.0)	8 (30.8)	< 0.001	5 (6.6)	3 (11.5)	0.425
RV dilation	7 (6.7)	0 (0.0)	7 (26.9)	< 0.001	5 (6.6)	2 (7.7)	1.000
Ventricular abnormality	24 (23.5)	0 (0.0)	24 (92.3)	< 0.001	14 (18.4)	10 (38.5)	0.034
TAPSE, cm	1.9 ± 0.3	2.0 ± 0.3	1.8 ± 0.2	0.159	2.0 ± 0.3	1.8 ± 0.2	0.045
FAC, %	35.2 ± 6.5	35.6 ± 6.0	34.1 ± 7.7	0.518	34.9 ± 6.5	36.4 ± 6.7	0.563
Significant MR	7 (6.9)	0 (0.0)	7 (26.9)	< 0.001	4 (5.3)	3 (11.5)	0.365
Significant TR	6 (5.9)	0 (0.0)	6 (23.1)	< 0.001	3 (3.9)	3 (11.5)	0.167
Significant AS	6 (5.9)	0 (0.0)	6 (23.1)	< 0.001	4 (5.3)	2 (7.7)	0.636
Significant valvulopathy	9 (8.8)	0 (0.0)	9 (34.6)	< 0.001	5 (6.6)	4 (15.4)	0.225
Pericardial effusion	6 (5.9)	0 (0.0)	6 (23.1)	< 0.001	3 (3.9)	3 (11.5)	0.171
Lung score	3.1 ± 2.4	2.9 ± 2.4	3.7 ± 2.5	0.119	2.7 ± 2.3	4.5 ± 2.4	0.001

Values are presented as mean ± SD or n (%).

AS, aortic stenosis; FAC, fractional area change; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; RV, right ventricular; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

* Abnormal echocardiogram was defined as left or right ventricular dysfunction or enlargement, or moderate/severe valvular regurgitation/stenosis echocardiographic study.

† *P* value for the difference between normal and abnormal echocardiograms.

‡ *P* value for the difference between advanced ventilatory support and no support.

Table 3. The association between abnormal echocardiogram and serious adverse events (end points)

Variable	All (n = 102)	Normal echocardiography (n = 76)	Abnormal echocardiography (n = 26)	*P* value	Unadjusted OR (95% CI)
Composite outcome*	20 (19.6)	8 (10.5)	12 (46.2)	< 0.001	7.29 (2.44-20.00)
In-hospital death	6 (5.9)	2 (2.6)	4 (15.4)	0.033	6.82 (1.2-39.7)
Mechanical ventilation	12 (11.8)	7 (9.2)	5 (19.2)	0.164	2.38 (0.68-8.29)
Shock	7 (6.9)	4 (5.3)	3 (11.5)	0.249	2.35 (0.5-11.3)
ADHF	6 (5.9)	0 (0.0)	6 (23.1)	0.005	22.8 (2.6-200.4)
Advanced ventilatory support	26 (25.5)	15 (19.7)	11 (42.3)	0.021	4.83 (1.5-15.3)
Myocardial injury	14 (13.7)	6 (7.9)	8 (30.8)	0.003	5.19 (1.6-19.9)
Chronic ventilation	9 (8.8)	6 (7.9)	3 (11.5)	0.414	1.52 (0.4-6.6)
Venous thromboembolism	3 (2.9)	2 (2.6)	1 (3.8)	1.000	1.48 (0.1-17.0)
Anti−COVID-19 drugs	40 (39.2)	27 (35.5)	13 (50.0)	0.192	1.82 (0.7-4.7)
Sepsis	11 (10.8)	6 (7.9)	5 (19.2)	0.108	2.78 (0.8-10.0)
Acute kidney injury	20 (19.6)	9 (11.8)	11 (42.3)	0.001	5.46 (1.9-15.5)
New renal replacement therapy	3 (2.9)	0 (0.0)	3 (11.5)	0.052	9.9 (0.98-99.9)
LOS, days	8.1 (3.0-16.3)	7 (2.8-14.1)	10.4 (6.8-29.3)	0.202	5.07 (−2.75-12.89)

Values are presented as n (%) or median (interquartile range).

ADHF, acute decompensated heart failure; CI, confidence interval; LOS, length of stay; OR, odds ratio.

*Composite outcome included in-hospital death, mechanical ventilation, shock, and acute decompensated heart failure.

a lower LVEF (49.2 ± 8.2% vs 57.2 ± 4.1%; $P < 0.001$), higher LVEDD (4.8 ± 0.6 cm vs 4.5 ± 0.5 cm; $P = 0.016$), and higher proportions of LVEF < 50%, RV systolic dysfunction and dilation, pericardial effusion, and significant valvulopathy (including significant mitral and tricuspid regurgitation and aortic stenosis). Comparing lung scores between patients with a normal echocardiogram and those with an abnormal echocardiogram yielded no association (2.9 ± 2.4 vs 3.7 ± 2.5; $P = 0.119$).

Four patients underwent an official echocardiography after the study examination during the index hospitalisation, which confirmed the findings of the focused echocardiogram.

Results among patients with and without advanced ventilatory support

Echocardiogram results and measurements among patients with and without advanced ventilatory support are presented in Table 2. Compared with patients with no advanced ventilatory support, patients with such support had a higher proportion of ventricular abnormalities (38.5% vs 18.4%; $P = 0.034$), a lower TAPSE (1.8 ± 0.2 cm vs 2.0 ± 0.3 cm; $P = 0.045$) and a higher lung score (4.5 ± 2.4 vs 2.7 ± 2.3; $P = 0.001$). The groups did not differ in other assessed or measured POCUS parameters.

Sensitivity and specificity among low- and high-risk patients

Among the 102 patients included in the study, only 32 were defined as low risk (with room-air oxygen saturation ≥ 94%), including 6 patients with abnormal echocardiograms, of which only 1 patient had the composite outcome. The sensitivity of focused echocardiography for the composite outcome among low-risk patients was 100% and the specificity 83.9% with PPV 16.7% and NPV 100%.

Among the 70 patients defined as high risk (with room-air oxygen saturation < 94%), the sensitivity of focused echocardiography for the composite outcome was 57.9% and the specificity 82.4% with PPV 55.0% and NPV 84.0%.

Association between abnormal echocardiogram and study end points

The associations between an abnormal echocardiogram and the end points are presented in Table 3 and Figure 1. An abnormal echocardiogram was associated with the end points of the need for advanced ventilatory support, ADHF, myocardial injury, acute kidney injury, death, and the composite end point (in-hospital death, mechanical ventilation, shock, and ADHF; unadjusted OR 7.29, 95% CI 2.44-20.00).

Multivariate analysis adjusting for age, heart failure, ischemic heart disease, smoking, hypertension, hyperlipidemia, previous revascularisation, cardiovascular implantable electronic device (CIED) implantation, or valve replacement revealed that among the entire cohort, an abnormal echocardiogram was independently associated with a higher probability for the composite end point (OR 6.19, 95% CI 1.50-25.57; $P = 0.012$).

Multivariate analysis adjusting for age, heart failure, hypertension, hyperlipidemia, smoking, and CIED implantation revealed that among high-risk patients, an abnormal echocardiogram was independently associated with a higher probability for the composite end point (OR 5.47, 95% CI 1.29-23.30; $P = 0.022$).

Association between lung score and study end points

The lung score was associated with the end points of the need for advanced ventilatory support, anti−COVID-19 medication use, myocardial injury, hospital length of stay, mechanical ventilation, ADHF, in-hospital death, and the composite end point (unadjusted OR 1.44, 95% CI 1.18-1.77).

Multivariate analysis adjusting for the above pertinent variables revealed that the continuous lung score was

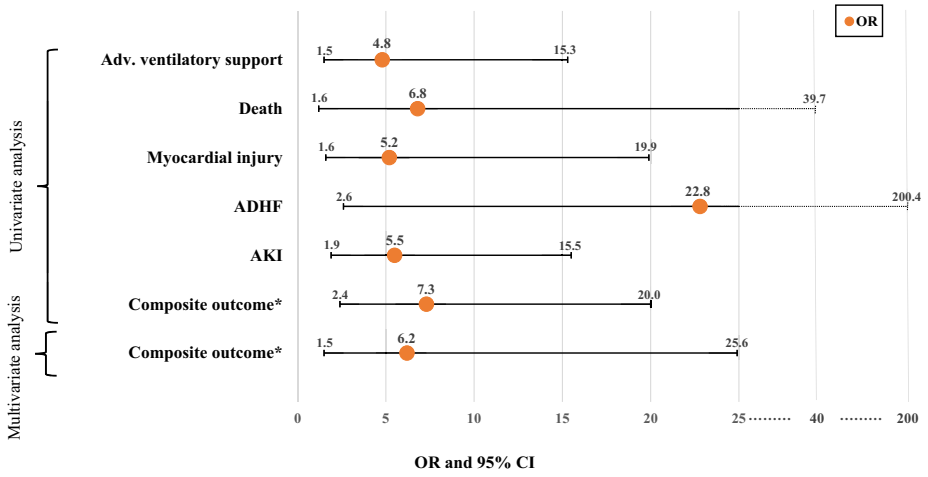

Figure 1. Significant associations (odds ratio [OR] and 95% confidence interval [CI]) between abnormal echocardiogram and serious adverse events (end points). *The primary end point was defined as a composite end point of in-hospital death, mechanical ventilation, shock, and acute decompensated heart failure. Numeric results of OR and 95% CI and are detailed in Table 3. ADHF, acute decompensated heart failure; Adv., advanced; AKI, acute kidney injury.

independently associated with a higher probability for the composite end point (OR 1.56, 95% CI 1.12-2.03; $P = 0.001$).

Discussion

This study is, to the best of our knowledge, the first to investigate the utility of handheld echocardiography in hospitalised patients with COVID-19 to predict end points based on identified cardiac abnormalities. Hospitalised patients with COVID-19 and an abnormal echocardiogram presented with a higher proportion of comorbidities and worse baseline functioning. Abnormal ventricular function/size or significant valvular pathology identified with the use of handheld ultrasound were associated with worse end points and were independently predictive of the composite end point of death, mechanical ventilation, shock, and ADHF. Also, the lung score with the use of a handheld ultrasound was associated with worse end points and was independently predictive of the composite end point. Among low-risk patients (with room-air oxygen saturation $\geq$ 94%) the prevalence of the composite end point was very low (3.1%) and focused echocardiography had a positive predictive value of only 14.3% in this group of patients.

COVID-19 is known to manifest a wide spectrum of cardiac pathologies and the use of echocardiography in these patients has an important role in the settings of myocarditis, acute coronary syndrome, cardiomyopathy, pericardial effusion, arrhythmia, and shock. Therefore, a timely echocardiogram is integral to the clinical evaluation and management of patients with COVID-19. The burden of the pandemic on health care systems necessitates achieving an appropriate balance between the relative necessity of the examination and the duty of sonographers, nurses, advanced practice providers, and physicians to provide high-quality imaging while limiting viral spread, reducing staff exposure, and protecting patients. In these settings, traditional criteria for echocardiography use seem too extensive and clinicians are required to prioritise the need for this valuable resource. The handheld devices have smaller nonsterile exposed areas compared with standard machines and can be easily decontaminated with disinfectant wipes, and their size allows for them to be entirely enclosed by a sterile covering to limit iatrogenic virus transmission.[12,13] The findings of the present study support the acquisition of a cardiac assessment sonographic tool that can be dedicated to the COVID-19 departments and can be operated more conveniently in accordance with recommended precautions.

An abnormal echocardiogram was observed in 25.5% of the study population. Other studies using standard cart-based machines or laptops and conducted on hospitalised patients with COVID-19 have found a relatively high rate of sonography-based cardiac abnormalities, ranging up to 68%, with RV systolic dysfunction being the most predominant finding (10%-52.8%).[14-20] This discrepancy may be explained by selection bias (patients with advanced illness), differing timelines between echocardiography and disease onset, lack of Doppler usage, partial RV visualisation, and discrepancies in the definition of an abnormal echocardiogram. Another important difference is the use of high-end devices or detailed full echocardiographic examinations in most of the studies. Because none of the studies used handheld ultrasound, their examination may be more meticulous but less practical in the COVID-19 clinical setting.

An example of studies focusing on patients with advanced illness is one in which an echocardiogram was performed only after approval by 3 physicians and on patients with elevated high-sensitivity troponin or a clinical need for the examination.[19] In that study, 82% of the patients required mechanical ventilation and 58% required vasopressor support. A correlation between disease severity and the prevalence of an

abnormal echocardiogram can be found in a cross-sectional study comparing patients with nonsevere COVID-19 and those with severe disease, demonstrating larger biventricular diameters alongside lower LVEF and RV fractional area change in those with severe disease.[21]

An association between mortality and cardiac abnormality on the echocardiogram was also found by Karagodin et al., who demonstrated an association between both LV and RV strain and mortality.[22] However, the routine use of strain for ventricular assessment is limited for patients hospitalised in COVID-19—designated departments. Also, unlike in our study, their cohort included a very high in-hospital mortality rate of 21.6%, which may reflect selection bias of patients with more severe COVID-19.

Study limitations

This was a prospective, single-centre, observational study and not a randomised trial, and as such is subjected to associated confounding factors. However, after constructing a multivariate analysis, the independent predictive value remained substantial. Also, data regarding previous echocardiographic examinations are lacking and not included in the analysis. Lack of pulsed- and continuous-wave Doppler usage and simultaneous electrocardiography limited the evaluation of valvular pathologies, hemodynamics, and echocardiographic images, which may have led to an underestimation of cardiac pathologies. Nonetheless, the study provides data in real-world settings that are relevant to the day-to-day limited clinical use of POCUS echocardiography in COVID-19 wards. A prospective POCUS study with noncardiologists vs cardiologists and low-risk vs high-risk patients would assist in clarifying the limitations of this study.

Conclusion

Abnormal echocardiographic results in hospitalised patients with COVID-19, when performed by a cardiologist or intensivist and interpreted by a fellowship-trained echocardiographer in a tertiary care setting, are associated with a higher burden of comorbidities and independently predict major adverse end points. Hand-held POCUS of hospitalised patients with COVID-19 can be utilized as an important "rule-out" tool among high-risk patients (with room-air oxygen saturation $< 94\%$) and should be integrated as part of their routine admission evaluation. The routine use of focused echocardiography among low-risk patients is not recommended for prognostication or as a screening tool.

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Disclosures

The authors have no conflicts of interest to disclose.

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