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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RESEARCH LETTER

Left ventricular ejection fraction: An additional risk marker in COVID-19

Fraction d'éjection ventriculaire gauche un marqueur de risqué additionnel dans la COVID-19

KEYWORDS
Echocardiography;
Coronavirus disease 2019;
Left ventricular ejection fraction

MOTS CLÉS
Echocardiographie ;
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Early identification of patients at high risk of death from COVID-19 [1] is a major issue for the management of patient flow and allocation of healthcare resources. Myocardial involvement has been highlighted as a powerful marker of increased hospital morbimortality in these patients [2], but the role of left ventricular function has not been fully investigated.

Methods

On 31 March 2020, our cardiology intensive care unit transitioned into a COVID-19 intensive care unit. Data from 39 consecutive patients admitted for acute pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) who had two-dimensional echocardiography performed on the day of admission were retrospectively analysed. Transthoracic echocardiography examinations were conducted respecting all protection rules and precautions [3], and the recordings were analysed completely off-line. Patients were divided into those who were intubated or died ($n = 12$) and those who did not experience an event (survivors without intubation) ($n = 27$) during the 15 days after admission.

Results

Mean age of the global population was 62 ± 14 years, 27 (69.2%) were men and median oxygen rate at admission was 6 L/min. Median time between admission to the intensive care unit and intubation/death was 5 days. Over 15 days of follow-up, 7 (17.9%) patients needed to be intubated and

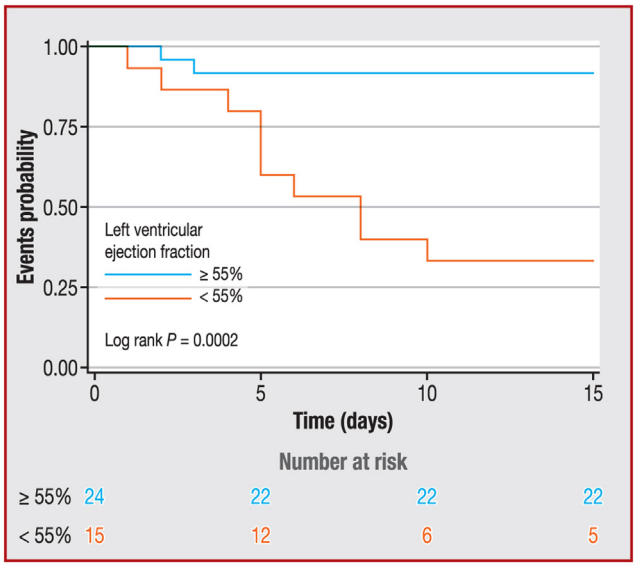

Figure 1. Kaplan-Meir survival curves for intubation or death at 15 days of follow-up according to left ventricular ejection fraction ≥ 55% or < 55%.

7 patients (17.9%) died, for a total of 12 (30.8%) endpoint events (intubations and/or deaths). The clinical, biological and echocardiographic characteristics of patients in the overall population and according to clinical outcome are displayed in the Table. At admission to intensive care, patients who underwent intubation or died, compared with survivors, had a significantly higher respiratory rate, lower haemoglobin level, higher C-reactive protein concentration, higher peak concentrations of cardiac biomarkers (high-sensitivity cardiac troponin and B-type natriuretic peptide), and lower left ventricular ejection fraction (all $P < 0.05$) (Table 1).

Kaplan-Meier analysis (Fig. 1) delineated the probability of the endpoint (intubation/death) according to a left ventricular ejection fraction cutoff of 55%. In multivariable stepwise Cox regression analysis, patients with a value < 55% had a hazard ratio of 10.18 (95% confidence interval, 2.17 — 47.87; $P = 0.003$) for death/intubation, independent of biological and clinical variables.

Discussion

In addition to clinical and biological factors, echocardiographic evaluation of left ventricular ejection fraction in patients with severe SARS-CoV-2 pneumonia could be of interest in refining their short-term prognosis.

Table 1 Clinical, biological and echocardiographic characteristics of patients with COVID-19 in the overall population and according to clinical outcome.

	Overall population ($n = 39$)	Survivors without intubation ($n = 27$)	Death/intubation ($n = 12$)	*P* value
Clinical characteristics				
Age (years)	62 ± 14	61 ± 13	66 ± 16	0.29
Male sex	27.0 (69.2)	17 (63.0)	10 (83.3)	0.28
Respiratory rate (breaths/min)	25 (22 – 34)	24 (21 – 30)	31 (25 – 36)	0.043
Hypertension	17.0 (43.6)	10 (37.0)	7 (58.3)	0.30
Diabetes	11.0 (28.2)	7 (25.9)	4 (33.3)	0.71
Dyslipidaemia	12.0 (30.8)	8 (29.6)	4 (33.3)	1.00
Obesity[a]	11.0 (28.2)	6 (23.1)	5 (41.7)	0.26
Current smoker	10.0 (25.6)	6 (23.1)	4 (33.3)	0.22
History of chronic cardiovascular disease	14.0 (35.9)	9 (33.3)	5 (41.6)	1
Laboratory findings				
Haemoglobin (g/dL)	14.0 (12.6 – 15.0)	14.4 (12.7 – 15.4)	12.7 (10.6 – 13.8)	0.007
Leucocytes ($\times 10^9$/L)	7.5 (5.7 – 9.7)	7.5 (5.7 – 9.7)	7.7 (5.4 – 11.5)	0.96
Lymphocytes ($\times 10^9$/L)	1.0 (0.6 – 1.5)	1.0 (0.7 – 1.7)	0.8 (0.6 – 1.4)	0.46
Fibrinogen (g/L)	6.3 (5.16 – 7.79)	6.3 (4.9 – 7.6)	7.6 (6.2 – 8.9)	0.10
D-dimers (mg/L)	1474 (634 – 2812)	1474 (513 – 2809)	1535 (955 – 2903)	0.71
eGFR (MDRD) (mL/min/1.73 m^2)	105 (82.0 – 127.0)	114.5 (94.5 – 126.5)	91.7 (59.0 – 123)	0.10
C-reactive protein (mg/L)	110.0 (34.6 – 210.0)	84.7 (25.0 – 156.0)	185.6 (123.8 – 298.0)	0.009
Procalcitonin (μg/mL)	0.1 (0.0 – 0.4)	0.1 (0.0 – 0.1)	0.4 (0.1 – 1.1)	
Hs-TnI (ng/mL)	14.0 (4.8 – 50.3)	11.0 (4.0 – 25.0)	20.0 (10.0 – 128.0)	0.09
Peak of hs-TnI (ng/mL)	15.5 (4.8 – 72.0)	11.0 (4.0 – 29.0)	96.0 (16.0 – 178.0)	0.02
BNP (pg/mL)	41.0 (10.5 – 209.0)	26.0 (8.8 – 163.8)	94.0 (39.0 – 756.0)	0.06
Peak BNP (pg/mL)	85.0 (12.0 – 399.5)	43.0 (8.8 – 220.5)	318.0 (59.0 – 1025.0)	0.02
Echocardiography				
Left heart				
LVEF (%)	59.7 (47.7 – 62.4)	61.0 (56.6 – 63.5)	51.2 (40.4 – 54.5)	0.001
Abnormal motion of left ventricle	11 (28.2)	5 (18.5)	6 (50.0)	0.06
Left atrial area (cm^2)	20.6 (16.9 – 26.0)	19.0 (15.7 – 26.6)	22.9 (19.4 – 26.4)	0.23
E/e'	8.6 (6.3 – 10.5)	8.8 (6.4 – 12.9)	7.2 (5.5 – 8.6)	0.11
Cardiac output (L/min)	5496 (4400 – 6259)	5482 (4400 – 6259)	5813 (4273 – 6967)	1.00
Right heart				
Right atrial area (cm^2)	14.3 (11.2 – 18.1)	14.4 (11.0 – 17.9)	13.9 (11.6 – 18.3)	0.77
RV basal diameter/LV basal diameter	0.8 (0.7 – 0.9)	0.8 (0.8 – 0.9)	0.8 (0.6 – 0.9)	0.90
FAC (%)	36.5 (28.6 – 41.2)	36.3 (28.6 – 41.1)	37.4 (27.4 – 54.8)	0.77
TAPSE (mm)	21.9 (17.5 – 25.0)	22.4 (17.2 – 25.8)	21.9 (17.0 – 23.6)	0.67
S' (cm/s)	12.3 (10.8 – 15.0)	12.6 (10.3 – 15.2)	12.0 (10.9 – 16.2)	0.86

Data are expressed as *n* (%), mean ± standard deviation or median (interquartile range). BNP: B-type natriuretic peptide; E/e': ratio between early mitral inflow velocity and mitral annular early diastolic velocity; eGFR: estimated glomerular filtration rate; FAC: fractional area change; hs-TnI: high-sensitivity troponin I; LV: left ventricular; LVEF: left ventricular ejection fraction; MDRD: Modification of Diet in Renal Disease; S': tricuspid lateral annular systolic velocity; TAPSE: tricuspid annular plane systolic excursion.
[a] Body mass index ≥ 25 kg/m^2.

Despite the increasing volume of data concerning the link between cardiovascular disease and severity of COVID-19, few studies have defined the role of echocardiography in risk stratification, and no data are available on the role of left ventricular function. First, it is important to highlight the importance of taking appropriate protective measures during the echocardiography examinations to avoid risk of contamination of both the sonographer and the physician. During our study, optimal protective precautions were used during each echocardiogram examination. Second, our study population was relatively young and had a high risk of complications (median oxygen rate was 6 L/min and respiratory rate was 25 breaths/min). Our results could have been different in a low-risk population (outpatients or non-intensive care unit management).

In the literature, left ventricular dysfunction has been reported in some cases of myocarditis and takotsubo syndrome. A recent study showed that right ventricular function

evaluated using strain imaging in a population of patients with COVID-19 with no history of cardiomyopathy was associated with a poorer prognosis [4]. Cardiac injury secondary to COVID-19 appears to be multifactorial. Some authors speculated on the mechanism through angiotensin converting enzyme 2 receptors, inflammatory over-reaction, vascular injury (microangiopathy, myocardial infarction), or cytokine storm [5]. So far, the difference between an acute myocardial injury directly linked with COVID-19 or an expression of an unknown atherothrombotic myocardial injury in a population with a high cardiovascular risk remains difficult.

Beyond the complexity of the mechanisms of cardiac involvement in patients with SARS-CoV-2 pneumonia, the non-invasive evaluation of left ventricular function, while respecting protection rules and precautions, could be a simple parameter to refine their short-term prognosis.

Disclosure of interest

The authors declare that they have no competing interest.

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