The Prognostic Impact of Myocardial Deformation Measures in Patients with COVID-19

João Giffoni Silveira Neto,[1] Marcello de Brito Campos,[2] Luiz Mello,[2] Marcela de Castro Giffoni,[3] Natanael Arnor da Silva Barros Goveia,[4] Antonio Claudio Lucas da Nóbrega,[1] Renata R. T. Castro[2]

Universidade Federal Fluminense,[1] Niterói, RJ – Brazil
Universidade Iguaçu,[2] Nova Iguacu, RJ – Brazil
PUC-Rio,[3] Rio de Janeiro, RJ – Brazil
Universidade Federal do Estado do Rio de Janeiro,[4] Rio de Janeiro, RJ – Brazil

Abstract

Background: **Cardiovascular involvement in COVID-19 has been extensively studied. Echocardiography is an important technique in identifying cardiac involvement, serving as an excellent tool for prognostic variables.**

Objectives: **Analyze the prognostic impact of speckle tracking in analyzing the left ventricle in patients with COVID-19 admitted to intensive care units (ICUs).**

Methods: **Patients diagnosed with COVID-19 admitted to the ICU underwent an echocardiographic examination within the first 48 hours of hospitalization and were divided into two groups according to hospital outcome (discharge or death). Conventional echocardiographic data, as well as global longitudinal strain of the left ventricle (LVGLS) and right ventricle (RVGLS) of both groups, were compared using Student's t test (for continuous variables) or the chi-square test (for categorical variables), considering $p < 0.05$ as statistically significant.**

Results: **The average age was 56 ± 14 years, and the proportion of men and women was similar. The mortality rate was 64%, more frequent in elderly patients and in patients with a higher number of comorbidities. LVGLS revealed lower values in patients who progressed to death, with a cutoff point below −18.1% (sensitivity = 90.4%, specificity = 96.6%) for this outcome, and, after multivariate statistical analysis, it was found to be the only statistically significant echocardiographic variable.**

Conclusion: **LVGLS is an important tool in the prognostic analysis of critically patients with COVID-19, offering a new window of possibilities for evaluating these patients.**

Keywords: **COVID-19; Echocardiography; Global Longitudinal Strain.**

Introduction

The evolving understanding of COVID-19, initially identified as an acute respiratory syndrome, has been expanded by studies revealing significant cardiovascular implications.[1-4] This raised pertinent questions about whether the presence of preexisting cardiovascular conditions is a risk factor for the severity and mortality of COVID-19, suggesting a vulnerability profile in affected patients,[5-10] or whether SARS-CoV-2 infection could induce cardiovascular complications even in individuals without a history of cardiac diseases.

In this context, two-dimensional echocardiography is particularly useful in the management of patients with COVID-19, especially given the prevalence of myocardial involvement in these infections. It provides valuable insights for defining cardiac involvement and patient management.[11-13] The use of myocardial strain techniques enhances these assessments through myocardial deformation analysis, a more sensitive approach than traditional volumetric assessments and ejection fractions, demonstrating high inter- and intraobserver reliability.[14-16]

We understand that the presence of early alterations in myocardial function, particularly related to subclinical systolic dysfunction of the left ventricle (LV), may be associated with poorer outcomes in patients affected by COVID-19. Consequently, the use of myocardial strain echocardiography (Central Illustration) becomes crucial in the initial assessment of these patients. Thus, the primary objective of this study is to investigate the prognostic impact of utilizing the speckle tracking technique in myocardial strain analysis for the evaluation of patients with COVID-19 infection. This includes describing LV function in patients admitted to intensive care units (ICUs) with COVID-19 and assessing the independent prognostic power of the speckle tracking technique in analyzing their LV function.

Correspondência: João Giffoni Silveira Neto •
Universidade Iguaçu. Av. Abílio Augusto Távora, 2134. CEP: 26275-580. Jardim Alvorada, Nova Iguaçu, RJ – Brasil
E-mail: joao.giffoni2@hotmail.com
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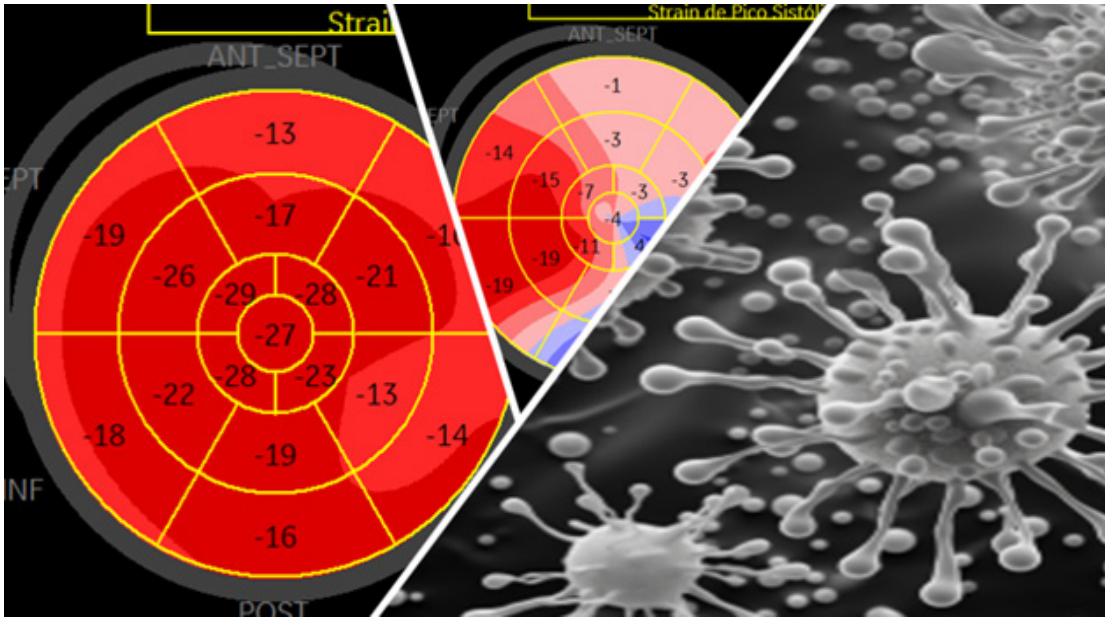
Central Illustration: The Prognostic Impact of Myocardial Deformation Measures in Patients with COVID-19



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Methods

Study design and population

This is a longitudinal, observational, and prospective study. For its execution, all patients admitted for COVID-19 infection to the ICUs of the Hospital Geral de Nova Iguaçu (HGNI) were recruited during the period from March 28 to December 30, 2020. The criteria for admission to these units included signs of severity and the need for mechanical ventilation.

The diagnosis of COVID-19 was confirmed with a positive result of real-time reverse transcriptase–polymerase chain reaction (RT-PCR) assay of pharyngeal swabs. All participants in the study underwent echocardiographic analysis within 48 hours of admission. Additionally, computed tomography (CT) scans of the lungs were performed.

Demographic data such as age, sex, ethnicity, weight, height, and known comorbidities were collected and cataloged alongside a questionnaire, which is provided in the annex. This included echocardiographic data and CT findings. The presence of comorbidities, such as hypertension or diabetes mellitus (DM), was reported by the patient themselves or, in cases where the patient was unable to respond (due to being sedated and intubated), the information was obtained from medical records or provided by a family member.

Patients were monitored throughout their hospital stay regarding the final in-hospital outcome (discharge, death, or transfer). This study did not interfere with the medical management during hospitalization and took into account that all care provided was in accordance with current best practices.

Criteria for ICU admission of patients

Patients admitted to the ICU with a diagnosis of COVID-19 were evaluated, based on RT-PCR tests conducted using respiratory secretion samples collected with a nasopharyngeal swab upon patient admission to the hospital, presenting signs or symptoms of SARS-CoV-2 infection. The tests utilized kits produced by Seegene Laboratory from the Republic of Korea, provided by the Brazilian Ministry of Health during that period. The assessment of signs or symptoms followed the guidelines of the Brazilian Ministry of Health's Clinical Management Protocol for COVID-19 in Specialized Care, as per the electronic version of the revised 1st edition of 2020.

Patients were considered severe if they demonstrated any of the following characteristics:[17]

a) Respiratory failure: significant breathing difficulty, characterized by dyspnea, hypoxemia (low blood oxygen level), or a high respiratory rate (tachypnea), and the need for supplemental oxygen support or mechanical ventilation;

b) Hemodynamic alterations: hypotension unresponsive to fluid resuscitation, presence of shock, whether septic, cardiogenic, or other types;

c) Consciousness alterations: confusion, disorientation, or reduced level of consciousness, which may indicate central nervous system involvement or metabolic encephalopathy;

d) Coagulopathies: evidence of disseminated intravascular coagulation or venous thromboembolism;

e) Chest imaging: progressive multilobar infiltrates in chest radiographs or CT with extensive pulmonary involvement.

Inclusion and Exclusion Criteria for Patients

The study included patients admitted to the HGNI during the study period (Table 1), of both sexes, aged 18 years and above, with a confirmed diagnosis of COVID-19 infection. Patients were excluded from the study if they died or were discharged from the hospital before the echocardiogram could be performed. Additionally, patients who were transferred to another hospital at any point during the study were also excluded, as such transfers made it impossible to follow up on patient outcomes. Patients who did not have echocardiographic images suitable for speckle tracking analysis were also excluded. There were no exclusions based on inconclusive results from the RT-PCR tests. All study patients underwent CT of the lungs.

Echocardiographic analysis

The echocardiographic evaluation of study participants was conducted within the first 48 hours following hospital admission. Images were collected using GE Healthcare Vivid IQ echocardiography equipment, employing a 3Sc-RS adult sector transducer from GE. The acquisition and analysis of echocardiographic data were performed by a single examiner with extensive experience. Image acquisition was conducted following the guidelines of the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EACVI).[11] All data were analyzed before the patient outcomes were known.

In the two-dimensional echocardiographic analysis, data were obtained on the diameters of the right and left heart, including left ventricle end-diastolic diameter (LVEDD), left ventricle end-systolic diameter (LVESD), a longitudinal cut of the long axis, as well as posterior wall in diastole (PWd), interventricular septum in diastole (IVSd), values used to obtain left ventricular mass (LVM) and relative wall thickness (RWT), calculated using the equation 2 × PWd/LVEDD. Additionally, the diameter of the right ventricle base was obtained by the apical 4-chamber (4C) view, with an emphasis on the right chambers.

In assessing LV diastolic function, via pulsed-wave Doppler of the transmitral flow in the apical 4C view, E-wave and A-wave velocities were obtained, along with the E/A ratio. The assessment of pulmonary artery systolic pressure (PASP), evaluated by the maximum velocity of tricuspid regurgitation via continuous-wave Doppler of tricuspid regurgitation flow, defines the maximum velocity of this flow squared, multiplied by 4, and is augmented by values based on the variation in diameter of the inferior vena cava, assessed in the subxiphoid view.

Analyses of left ventricular global longitudinal myocardial deformation (LVGLS) were performed using images acquired from the apical long-axis in four, two, and three chambers. These images were transferred to an offline analysis platform (EchoPAC Software Only v 202), where they were processed for study. Peak systolic strain was defined as the point of maximum systolic shortening for longitudinal deformation. Aortic valve closure was used as a reference point to define the end of systole with speckle tracking.

Left ventricular ejection fraction (LVEF) analysis was conducted using the biplane Simpson's technique, through 4C and 2C views, and the analysis of LVGLS, applying as cutoff points abnormal values for LVEF (< 52% for men and < 54% for women) and LVGLS < 18% for both sexes. Right ventricular function was analyzed by tricuspid annular plane systolic excursion (TAPSE), via the apical 4C view with an emphasis on the right chambers, with abnormal cutoff values being < 17 mm. Furthermore, global longitudinal strain of the right ventricle (RVGLS) was also analyzed offline using EchoPAC Software Only v 202, with abnormal cutoff values of < 20%.

Normal values for echocardiographic variables in relation to sex and also biventricular myocardial strain can be observed in Table 2 and followed the guidance of the Recommendations for Chamber Quantification by Echocardiography in Adults by the ASE and the EACVI[11] and the Position Statement on the Use of Myocardial Strain in Cardiology Routines by the Brazilian Society of Cardiology's Department Of Cardiovascular Imaging.[16]

Chest CT

Patients underwent pulmonary CT evaluation within the first 48 hours of admission, using a Toshiba Alexion 16-channel CT scanner. Moreover, their images were processed for assessment on a K-Pacs reporting system. The multinational consensus of the Fleischner Society[18] was utilized, where an experienced radiologist performed the analyses, classifying the pulmonary involvement in patients as mild (pulmonary involvement < 25%), moderate (pulmonary

Table 1 – Inclusion and exclusion criteria for patients in the study

Patients included in the study	Patients excluded from the study
Admitted to the ICU of HGNI with a diagnosis of COVID-19	Died before undergoing echocardiography
Diagnosed with COVID-19 via RT-PCR	Transferred to another healthcare facility, precluding outcome follow-up
Underwent CT of the lungs	Inconclusive COVID-19 diagnosis
Echocardiographic examination conducted within 48 hours of ICU admission	Echocardiographic images unsuitable for speckle tracking strain analysis
Aged 18 years and older	Under 18 years old

HGNI: Hospital Geral de Nova Iguaçu; ICU: intensive care unit; RT-PCR: reverse transcriptase–polymerase chain reaction; CT: computed tomography.

Table 2 – Reference values for normality of echocardiographic variables and biventricular longitudinal strain values

Echocardiographic parameter	Reference value – male	Reference value – female
IVSd, mm	Up to 11	Up to 11
LVEDD, mm	42 to 58.4	37.8 to 52.2
LVESD, mm	25 to 39.8	21.6 to 34.8
PWd, mm	Up to 11	Up to 11
LVEF, %	52% to 72%	54% to 74%
LVM, g	88 to 224	67 to 162
RVBD, mm	25 to 41	25 to 41
TAPSE, mm	≥ 17	≥17
LVGLS, %	> 18%	> 18%
RVGLS, %	> 20%	> 20%

IVSd: interventricular septum in diastole; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVGLS: left ventricular global longitudinal strain; LVM: left ventricular mass; PWd: posterior wall in diastole; RVBD: right ventricular base diameter; RVGLS: right ventricular global longitudinal strain; TAPSE: tricuspid annular plane systolic excursion.

involvement between 25% and 50%), and severe (pulmonary involvement > 50%).

Statistical analysis

Echocardiographic, CT, clinical, and epidemiological variables were analyzed for the normality of their distribution using the Kolmogorov-Smirnov test. Since all data showed a normal distribution, continuous variables were presented as mean ± standard deviation, and categorical variables were reported as proportions.

The variables of patients who were discharged (discharge group) or who passed away (death group) were compared using the unpaired two-tailed Student's t test (for continuous variables) or the chi-square test (for categorical variables), or their non-parametric equivalents, when applicable.

The assumptions of the Cox model were verified, including the proportionality of hazards, which was confirmed through the Schoenfeld test ($p > 0.05$) and residual plots. There was no indication of multicollinearity (VIF < 10 for all covariates), and the sample size was considered sufficient, with an adequate number of events for each covariate. Therefore, we proceeded with the analysis of the independent prognostic power of each studied variable by constructing several Cox regression analysis models.

To test the independent prognostic power of each variable under study, various multiple regression analysis models were constructed. Echocardiographic variables that retained their independent prognostic power in the multiple regression analysis were used to construct ROC (receiver operating characteristic) curves, using hospital mortality as the outcome. Thereafter, cutoff points and their sensitivity, specificity, and area under the curve were calculated for each of these parameters. The best balance between sensitivity and specificity defined the cutoff point for the variables used to construct the Kaplan-Meier survival curve.

A two-tailed p value of < 0.05 was considered significant. All statistical analyses were conducted using STATA 14.2 software (StataCorp, Texas, USA).

Results

During the period from March 28 to December 30, 2020, 174 patients admitted to the ICU of HGNI were analyzed. Of these, 24 patients did not have adequate echocardiographic imaging for the study of myocardial deformation, accounting for 13.8% of the total. The in-hospital mortality rate among the patients included in the study was high (64%), as demonstrated in Figure 1.

Demographic data, CT, and presence of comorbidities

Among the 150 patients included in this study, as described in Table 3, the mean age was 56 ± 14 years, with 77 (51.3%) being male. The majority (77.3%) of the patients exhibited over 50% pulmonary involvement. Regarding comorbidities, hypertension was the most prevalent (84%), followed by obesity (41.3%), and DM (34%).

Patients who died had a higher mean age (59 ± 15 versus 50 ± 12 years, $p < 0.001$) and more comorbidities compared to those who were discharged (Table 3). A clear difference was observed in age and comorbidities when both groups were compared in the univariate analysis (Table 3). However, after multivariate regression analysis of the demographic parameters, only the presence of more than 50% pulmonary involvement on tomography remained as an independent predictor of in-hospital mortality (Figure 2).

Echocardiographic parameters

Patients who died had larger ventricular dimensions and a lower LVEF compared to patients who were discharged (Table 4). Only 36% of the patients who died had an abnormal LVEF, while only 2% of the patients who were discharged presented with an abnormal LVEF.

Considering a cutoff point of 40% for LVEF, 16% of the patients who died had an alteration while none of the discharged patients presented this condition ($p = 0.002$) (Table 5).

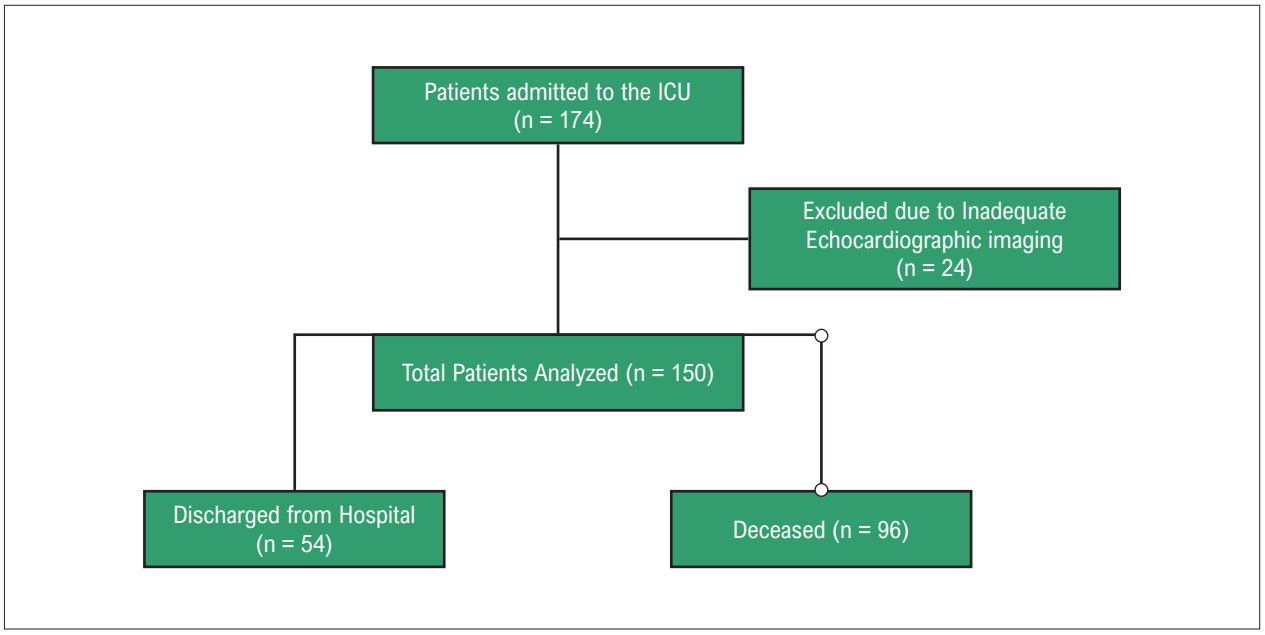

Figure 1 – *Flow diagram of patients included in the study. ICU: intensive care unit.*

Table 3 – Demographic data, presence of comorbidities, and pulmonary involvement of patients included in the study

Parameter	Total patients (n = 150)	Patients discharged (n = 54)	Patients who died (n = 96)	p value
Age (years)	56 ± 14	50 ± 12	59 ± 15	<0.001
Male sex [n (%)]	77 (51.3%)	30 (56%)	47 (49%)	0.44
Pulmonary involvement >50% on CT [n (%)]	116 (77.3%)	26 (48%)	90 (94%)	<0.001
Obesity [n (%)]	62 (41.3%)	13 (24%)	49 (51%)	<0.001
Hypertension [n (%)]	126 (84.0%)	36 (67%)	90 (94%)	<0.001
DM [n (%)]	51 (34.0%)	4 (7%)	47 (49%)	<0.001

CT: computed tomography; DM: diabetes mellitus.

Among the patients who died, 30% had an increased right ventricular base diameter, in contrast to only 1.85% of discharged patients who exhibited the same increase. Regarding the LVEDD, 26% of the patients who died had elevated values for this parameter, while, among those discharged, only 3.7% showed an increase in LVEDD. These data suggest a correlation between the enlargement of these measurements and a negative outcome during hospitalization for COVID-19.

The comparison of LVGLS revealed lower values in patients who died compared to those who were discharged (15.3 ± 2.3 versus 19.7 ± 1.8, $p < 0.001$). Similarly, the RVGLS was also lower in patients who died (21.9 ± 4.2 versus 28.0 ± 3.2, $p<0.001$).

The Cox multivariate analysis indicated that only the LVGLS and more than 50% tomographic involvement remained as independent prognostic predictor variables (Figure 3). Notably, none of the conventional echocardiography variables emerged as independent predictors of prognosis after multivariate analysis.

A cutoff point of −18.1 was used for the LVGLS in constructing the intra-hospital survival curves ($p < 0.001$; confidence interval 0.53 to 0.23) (Figure 4).

Discussion

Since echocardiography was identified as a relevant technique for managing patients with COVID-19, numerous questions and hypotheses have emerged, leading to the development of extensive research worldwide. In this context, our study demonstrated that LVGLS emerged as an independent prognostic marker in patients hospitalized in ICUs due to COVID-19.

With the advancement of these research efforts, certain variables were identified that directly correlate with the outcome of death. The ECHOVID-19 study[19] evaluated 214 hospitalized COVID-19 patients without severe criteria and conducted a paired analysis with 214 control patients without a COVID-19 diagnosis. After excluding patients with

LVEF < 40%, the authors concluded that reduced LVGLS and elevated TAPSE were prognostic predictors with cutoff points of 16.7% and 24 mm, respectively. This presents a divergence from our study where TAPSE did not show independent prognostic power, and the cutoff for LVGLS was set at less than 18.1%. This indicates that not only the COVID-19 infection itself but also the severity of the patient at the time of admission and the timing of the examination can directly influence the initial analysis. A systematic review and meta-analysis[20] also assessed the association between TAPSE and mortality in patients with COVID-19, concluding that lower TAPSE values were associated with higher mortality, with each percentage point decrease resulting in a 20% increased chance of death. However, a specific cutoff point was not provided. Additionally, there were variations among the patient populations used in the meta-analysis, including outpatient groups and more critical patient groups, with variable admission times and examination timings.

In April 2022, Gomez et al.[21] assessed echocardiographic predictors of mortality and morbidity in critical COVID-19 patients, analyzing the death outcome over a 60-day hospitalization period. They observed that abnormalities in the right ventricular echocardiographic parameters significantly impacted patient prognosis. Patients with right ventricular dilation had twice the risk of 60-day mortality due to COVID-19, and after multivariate analysis, the right ventricular basal diameter was the only statistically significant variable. However, the timing of the echocardiographic examinations was not specified in their methods, an important factor for understanding the analysis.

Despite the larger values of the right ventricular base diameter and TAPSE observed in patients who died, these variables did not demonstrate independent prognostic power in our study. This could be due to the early collection of data, within 48 hours of admission, meaning this involvement might not have fully manifested, supporting the notion that echocardiographic alterations in the right chambers may become more apparent over the course of hospitalization. This progression can indicate a worsening of the condition, leading to a more unfavorable prognosis.

In studies evaluating LV myocardial deformation in COVID-19 patients, Bhatia et al.[22] demonstrated that, although conventional echocardiographic parameters are important, they may not be sufficient. In these studies, despite normal LVEF, patients with greater severity exhibited significantly reduced LVGLS.

Regarding the use of LV deformation values as mortality predictors, Park et al.[23] concluded that an LV deformation value of <13.8% was an independent predictor of mortality in hospitalized patients, with a sensitivity of 85% and specificity of 54%. It was also a strong marker of survival. However, the

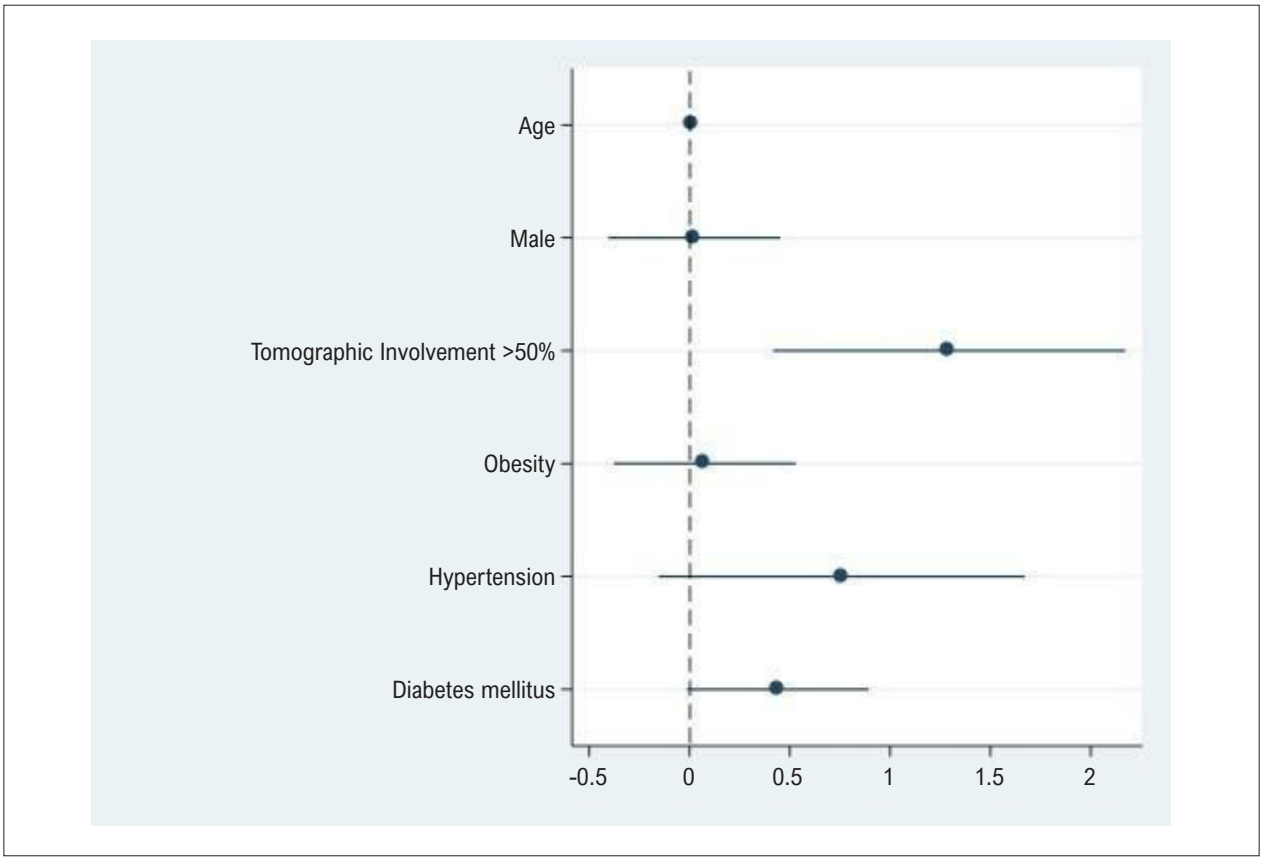

Figure 2 – *Multivariate Cox regression analysis of demographic parameters, pulmonary involvement on CT, and the presence of comorbidities, considering the outcome of in-hospital mortality*

Table 4 – Echocardiographic parameters within the first 48 hours of ICU admission in COVID-19 patients who were discharged and those who died during hospitalization

Echocardiographic parameter	Patients discharged (n = 54)	Patients who died (n = 96)	p value
IVSd (mm)	8.1 ± 0.8	8.7 ± 1.3	0.009
LVEDD (mm)	47.2 ± 4.4	50.2 ± 7.8	0.010
LVESD (mm)	29.8 ± 2.8	35.3 ± 8.7	<0.001
PWd (mm)	8.2 ± 0.7	8.9 ± 1.4	<0.001
LVEF (Simpson's biplane, %)	66 ± 4	57 ± 12	<0.001
E wave (cm/s)	0.7 ± 0.2	0.6 ± 0.2	<0.001
A wave (cm/s)	0.7 ± 0.2	0.7 ± 0.2	0.36
LVM (g)	161.2 ± 36.5	195.7 ± 63.0	<0.001
E/A ratio	1.1 ± 0.4	0.9 ± 0.6	0.032
RVBD (mm)	32.3 ± 3.0	37.2 ± 6.1	<0.001
PASP (mmHg)	23.6 ± 4.0	34.0 ± 10.8	<0.001
TAPSE (mm)	22.2 ± 2.3	19.4 ± 3.2	<0.001

IVSd: interventricular septum in diastole; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVM: left ventricular mass; PASP: pulmonary artery systolic pressure; PWd: posterior wall in diastole; RVBD: right ventricular base diameter; TAPSE: tricuspid annular plane systolic excursion.

Table 5 – Frequency of altered echocardiographic parameters within the first 48 hours of ICU admission in COVID-19 patients who were discharged and those who died during hospitalization

Echocardiographic parameter	Patients discharged (n = 54)	Patients who died (n = 96)	p value
Normal IVSd (mm)	54 (100)	94 (98)	0.29
LVEDD (mm)	53 (98)	71 (74)	<0.001
PW [n(%)]	54 (100)	91 (95)	0.088
LVEF [n(%)]	53 (98%)	67 (70%)	<0.001
LVEF < 40% [n(%)]	54 (100%)	81 (84%)	0.002
LVM [n(%)]	42 (78)	48 (50)	<0.001
E/A ratio [n(%)]	23 (43)	65 (68)	0.003
RVBD n(%)]	53 (98)	69 (72)	<0.001
PASP [n(%)]	40 (74)	36 (38)	<0.001

IVSd: interventricular septum in diastole; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVM: left ventricular mass; PASP: pulmonary artery systolic pressure; PW: posterior wall; RVBD: right ventricular base diameter.

timing of the echocardiographic analysis in this study was not specified, which could account for the difference compared to our data.

Rothschild et al.[24] defined an LV deformation value of 16.6% as a predictor for mortality and the need for intubation in admitted patients. A strength of this study was performing the echocardiographic transthoracic test within the first 24 hours of admission. It is common in studies to find a correlation between the presence of subclinical dysfunction and normal LVEF values by two-dimensional echocardiographic analysis.[23,24]

These findings corroborate those of the present research, demonstrating that the evaluation of strain is extremely important in defining ventricular function and in identifying cutoff points of LV deformation as predictors of mortality and survival curves.

In our study, we identified that echocardiographic analysis can provide various important variables in assessing patients with severe COVID-19. However, alteration in LVGLS was the only echocardiographic variable that could predict prognosis in patients hospitalized in intensive care with COVID-19 infection.

COVID-19 infection has raised many questions regarding the progression of affected patients. Various pathologies have been associated with worse prognoses, rapid disease progression, and overall disease severity. However, understanding whether merely possessing a risk factor is indicative of a more severe disease course has been and continues to be the focus of extensive research.

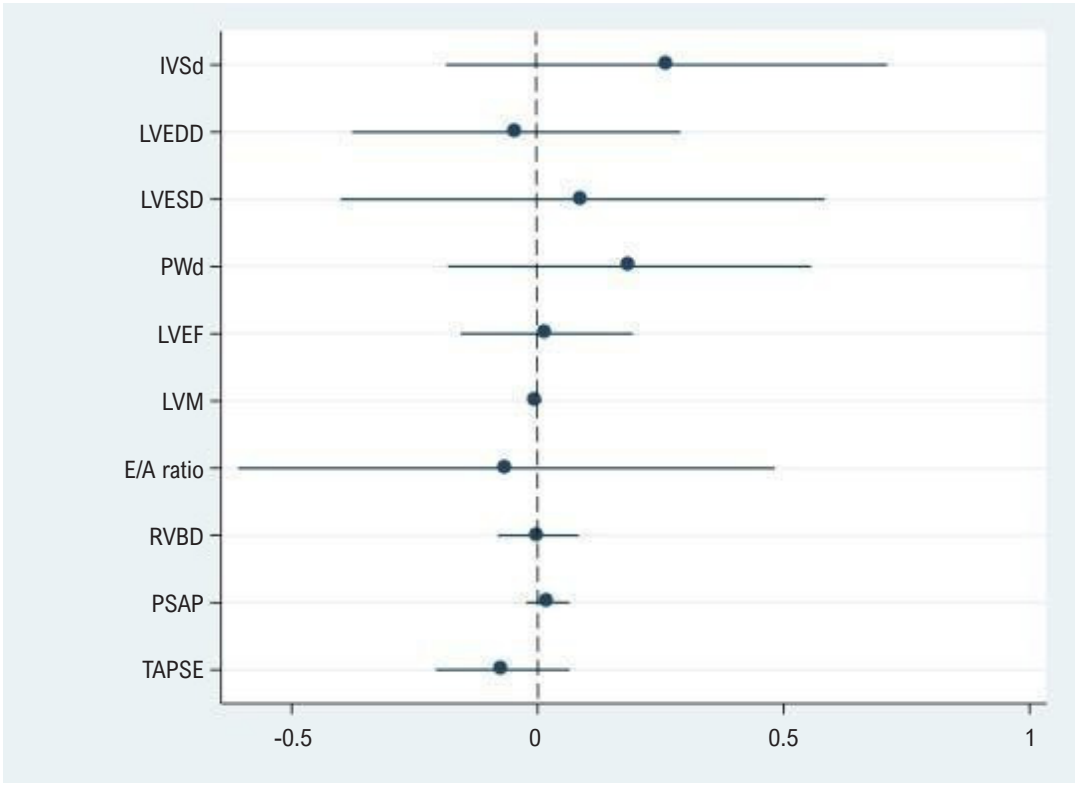

Figure 3 – *Multivariate Cox regression analysis of two-dimensional echocardiogram parameters, considering the outcome of in-hospital mortality. IVSd: interventricular septum in diastole with normal values; LVEDD: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVM: left ventricular mass; PASP: pulmonary artery systolic pressure; PWd: posterior wall in diastole; RVBD: right ventricular base diameter; TAPSE: tricuspid annular plane systolic excursion.*

This study observed that the prevalence of a more aggressive disease course was associated with the presence of risk factors; however, having some degree of cardiac structural or functional alteration was found to be more relevant than merely having hypertension, DM, obesity, or belonging to a specific sex. Even the presence of biomarkers indicating cardiac injury was less significant.

This line of reasoning leads to another question: understanding which type of echocardiographic technique should be used to define LV function in COVID-19 patients. In this context, the use of echocardiography, with myocardial deformation analysis, emerges as a viable option to define the presence or absence of myocardial dysfunction early on. This approach can then truly determine whether an isolated risk factor is associated with a worse prognosis of COVID-19.

Limitations

Regarding the limitations of this study, it is important to note that the analyzed patients were admitted to the ICU, and the study group thus represented cases with more severe COVID-19 progression. Nonetheless, it was possible to identify patients with higher severity who eventually succumbed to in-hospital mortality.

One of the primary challenges encountered was the difficulty in positioning patients in bed to achieve the necessary angulation for optimal image acquisition. This issue, compounded by the chaotic environment caused by the pandemic, led to inadequate imaging for some patients. Similar difficulties in image collection have been reported in ICUs by Croft et al.[25] where 53.7% of patients were excluded due to inadequate images. Additionally, Krishnamoorthy et al.[26] excluded 88.4% of their patients, and Lassen et al.[27] had only 9.3% of their patients excluded for inadequate images, although their examinations were conducted on an outpatient basis.

The correlation between myocardial dysfunction and cardiac injury biomarkers could not be performed in all patients, due to the lack of resources in the unit for conducting laboratory tests within the first 48 hours of admission. Additionally, the unavailability of other supplies precluded the analysis of other markers such as PCR, D-dimer, and interleukins, which were not included in the study.

There was also no correlation made with the drugs used in treatment due to the high divergence in treatments at the time, as it was a period of learning and experimentation in this regard. However, it is important to note that the researchers

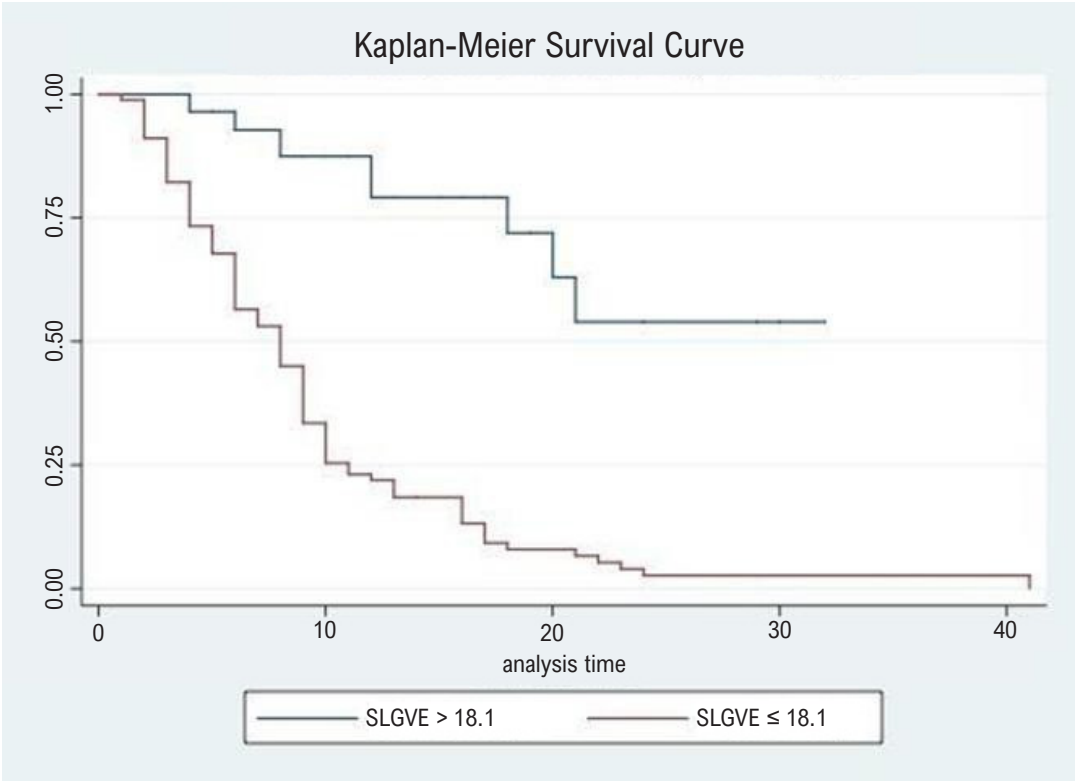

Figure 4 – *Kaplan-Meier survival curve based on left ventricular global longitudinal strain. LVGLS: left ventricular global longitudinal strain.*

did not interfere with the therapeutic conduct, and all patients were treated according to the best practices available during that period.

The measurement of systolic and diastolic blood pressure was not included in our data due to the wide variety of sphygmomanometer models in the unit. Even if the echocardiographic examiner wished to perform the pressure measurement at the time of the exam, there was no universal understanding at that time about the management and use of these devices among patients.

Among all the difficulties encountered, the greatest was undoubtedly related to the timing of the research, as we were living under the shadow of insecurity and uncertainty caused by a lack of knowledge, along with a constant fear that dominated the environment. Even though motivated by the necessity of discovery and the production of knowledge to assist the population, these conditions significantly hampered the research process.

Conclusion

We have determined that two-dimensional echocardiography has limited value for routine screening in patients hospitalized with COVID-19, not presenting specific variables that could contribute to prognostic analysis. Even when these variables show statistical significance, they are within the normal range, leading to interpretative ambiguities.

In this context, LVGLS demonstrates high levels of sensitivity and specificity, making it a reliable tool for prognostic evaluation in patients hospitalized in serious condition with COVID-19 infection.

In the fight against COVID-19, it is essential to identify patients at greater risk of developing severe forms of the disease. In addition to existing comorbidities, the prior condition of cardiac function emerges as a decisive factor in risk stratification. Therefore, meticulous analysis is crucial for a more precise risk assessment.

Author Contributions

Conception and design of the research: Silveira Neto JG, Giffoni MC, Nóbrega AC, Castro RRT; acquisition of data: Silveira Neto JG, Campos MB, Mello L, Giffoni MC, Goveia NASB; analysis and interpretation of the data: Silveira Neto JG, Campos MB, Nóbrega AC, Castro RRT; statistical analysis and critical revision of the manuscript for intellectual content: Silveira Neto JG, Nóbrega AC, Castro RRT; writing of the manuscript: Silveira Neto JG, Campos MB, Giffoni MC, Castro RRT.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee on Animal Experiments of the Universidade Iguaçu under the protocol number 39511820.5.0000.8044.

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