Original article

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Transthoracic echocardiography outcomes in critical COVID-19 and association with symptom burden - a longitudinal cohort study

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Abstract

***Objective*: To look for any relationship between severe/critical coronavirus disease 2019 (COVID-19) illness and post-discharge cardiac function, and also assess any correlation between this and post-COVID symptom burden.**

***Design*: Observational cohort study with both retrospective and prospective components.**

***Setting*: Intensive Care Unit (ICU) and subsequent outpatient clinic at a tertiary hospital in Western Sydney, New South Wales (NSW), Australia.**

***Patients*: All patients admitted to the ICU with COVID-19 infection between 01 July 2021 and 31 December 2021 were included (n=89).**

***Interventions*: The cohort was divided into survivors (n=61) and non-survivors (n=28). Those who underwent transthoracic echocardiography (TTE) (survivors, n=22; and non-survivors, n=23). The survivors who had an inpatient TTE were invited back for a repeat TTE and standardised symptom assessment questionnaire (COVID-19 Yorkshire Rehabilitation Scale [C19-YRS]). For all patients, demographic, clinical, biochemical, and pharmacologic data was collected.**

***Measurements and results*: Eighty-nine patients were included in the initial dataset, of which 45 had a TTE whilst acutely unwell, and 22/45 survived to hospital discharge. There were no significant differences in the measured TTE parameters between survivors and non-survivors. Of the survivors with a follow-up TTE, the majority of the changes seen in the initial study had resolved. Despite this, there was still an appreciable symptom burden in the domains of fatigue, breathlessness, ability to independently do activities of daily living, and overall reduced perception of health.**

***Conclusions*: In a cohort of critically unwell COVID-19 patients, there were no significant echocardiographic differences between survivors and non-survivors. For the survivors, whilst the majority of acute cardiac changes associated with COVID-19 infection resolved over time, however, there remained a significant symptom burden, including breathlessness and fatigability, suggesting a non-cardiac aetiology of these symptoms.**

Key words: Critical illness, echocardiography, COVID-19.

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Introduction

Acute cardiac complications of severe coronavirus disease 2019 (COVID-19) infection are diverse; however, the persistence of these changes and correlation with ongoing symptoms (post acute-COVID syndrome) is unclear. Direct myocardial injury and/or myocarditis can result in ongoing morphologic and functional cardiac changes, with case reports documenting myocardial oedema, reduced systolic function, pericardial effusions, and intramural fibrosis in the post-infection period. (1) The risk of ischaemic and non-ischaemic cardiac dis-

ease, dysrhythmia, cardiomyopathy, and heart failure are all increased post-COVID-19 infection compared to matched controls, with the risk increase proportional to disease severity. (2,3) Whilst cardiac magnetic resonance imaging (CMRI) has been used to identify early and late convalescent changes, (4) widespread use of this imaging modality is not a feasible approach in Australia due to resource limitations.

Transthoracic echocardiography (TTE) can be used for real-time assessment of direct and indirect cardiac changes, including left ventricular (LV) and/or right ventricular (RV) systolic dysfunction, diastolic dysfunction, raised pulmonary artery pressure, and myocarditis. (5,6) TTE has been used extensively in the assessment of patients with COVID-19: the largest dataset (1216 patients) published to date assessing echo parameters in acute COVID-19 showed that over half of patients (53%) had an abnormal echocardiogram. Of this cohort, almost half (46%) had only mild or moderate severity COVID-19 disease, with there being no additional data about the severe disease subgroup. (7) The recently published ECHO-COVID study looked at 667 intensive care unit (ICU) patients with COVID-19, demonstrating RV systolic dysfunction in 22.5%, LV systolic dysfunction in 22%, and acute cor pulmonale (ACP) in 19.5%. (8)

Given the extent of cardiac involvement in severe COVID-19 coupled with the increased risk of long-term cardiac sequelae associated with severe COVID-19, a structured follow-up program for patients with acute cardiac anomalies in the setting of COVID-19 infection should be considered. Here we present the clinical and TTE features of a cohort of patients with severe COVID-19 respiratory disease that required ICU admission. For the survivors, we present follow-up TTE and post-COVID-19 symptom questionnaire data (COVID-19 Yorkshire Rehabilitation Scale [C19-YRS], a multi-domain symptom assessment tool) to report ongoing post-COVID-19 disease burden, which may be associated with cardiac dysfunction. (9)

Materials and methods

Retrospective single centre cohort study including all patients admitted to the ICU of a 520-bed tertiary referral hospital between July 1st, 2021 and December 31st, 2021, with a confirmed diagnosis of COVID-19. Patients were divided into four cohorts as outlined in **Figure 1**: cohort one - survivors to discharge who had a TTE in ICU; cohort two - survivors to discharge that did not have a TTE in ICU; cohort three - died in ICU and had a TTE; cohort four - died in ICU and did not have a TTE. As extracorporeal membrane oxygenation (ECMO) can be initiated but not maintained at the involved hospital. All patients who were transitioned to ECMO were followed to the time of death or discharge from the ECMO centre.

Echocardiography

Scans were performed by qualified cardiac sonographers or intensive care fellows undertaking an advanced echo qualification and reviewed by the reporting doctor for the echo lab. A standard protocol based on the American Society of Echocardiography 2019 guidelines was followed. (10) Where patients had multiple transthoracic studies during their ICU stay, only the first comprehensive study was included for analysis. Follow-up transthoracic studies occurred in the outpatient echocardiography suites within the hospital.

Echo data was reviewed from the image storage and analysis software EchoPACS (GE). Demographic and clinical data were taken from custom electronic medical record software utilised in the local ICU (Intensys).

C19-YRS data

C19-YRS is a public domain, twenty-two-item patient-reported outcome measure that assesses the long-term impact of COVID-19 across the activity and participation domains of the International Classification of Functioning, Disability and Health that is commonly used in post-COVID clinics. (11-13) It has an overall health domain (zero-ten, where zero represents the worst possible health imaginable for the patient and ten the best possible health) as well as a series of symptom-specific questions graded on a reversed zero-ten scale (where zero represents no symptom burden or functional limitation and ten represents severe symptoms/complete dependence).

C19-YRS data was collected from cohort one patients by specialist physicians (combination respiratory, cardiology, infectious diseases, and rehabilitation specialties) through the hospital post-COVID clinic in a combination of both telehealth and face-to-face clinical interviews. C19-YRS data is presented in before-after dot plot format divided across domains.

Data analysis

Data analysis was performed using GraphPad Prism 9 and Jamovi version 2.0.0.0. For continuous data, the descriptive statistics are presented as median (interquartile range) due to the small sample size and data being non-parametric. Categorical data are presented as numbers (%). Box plots are presented

with median (horizontal line) and mean (black square). Statistical analysis was performed using Mann-Whitney U and Wilcoxon tests (for paired samples). Group comparisons with the Kruskal-Wallis test for continuous variables, chi-squared for categorical variables, and Fisher's exact test where n<5. Between-group pairwise comparisons were performed with the Dwass-Steel-Critchlow-Fligner pairwise comparison method.

This study was approved by the Nepean and Blue Mountains Local Health District ethics committee (2021/ETH11687).

Results

ICU study population

There were eighty-nine COVID-19 patients requiring ICU admission during the study period, of which forty-five (51%) had a TTE. The study population had a median age of forty-nine (20) years and a median body mass index (BMI) of 33.5 (13.4) (n=87). Fifty-five (62%) were male and forty-one (46%) had at least one comorbidity, with diabetes mellitus being the most common (n=29, 33%). The incidence of comorbidities was higher in non-survivors. **Table 1** demonstrates the patient and clinical characteristics of each cohort.

Eighty-seven (98%) patients received glucocorticoids, seventy-one (80%) patients received remdesivir, and sixty-four (72%) received immunomodulatory therapy in the form of tocilizumab or baricitinib.

Sixty-three (71%) of patients received non-invasive ventilatory support in the form of either continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP), and thirty-eight (43%) of patients received invasive ventilation.

There was a statistically significant difference in the median length of ICU stay, being greatest in cohort three (213.6 [IQR 286.2] hours) and shortest in cohort four (29.7 [65.2] hours) (p<0.001). The median hospital stay was greatest in cohort one (516 [364.7] hours) and least in cohort four (164.9 [149.5] hours) (p=0.0048) (**Figure 2A-B**).

Echocardiographic features

A summary of the echo findings and the relevant summary statistics for cohorts one and three are presented in **Table 2**. Not all reported measures were obtained for each patient. There was no significant difference between any of the measured indices between survivors and non-survivors. The majority of patients (n=43, 96%) had image quality suitable for subjective assessment of biventricular function, with the most common finding for both cohorts being normal left ventricular systolic function (cohort one 14/21, 67%; cohort three 14/22, 64%) and normal right ventricular systolic function (cohort one 17/21, 81%; cohort three 19/22, 86%).

RV-PA coupling (defined as tricuspid annular plane systolic excursion [TAPSE]/systolic pulmonary artery pressure [sPAP]) had a median value of 0.98 (1.28) for cohort one and 0.59 (2.03) for cohort three (p=0.11). This is reflective of a median TAPSE within normal limits (19 cm/s [7] in cohort one and 21 cm/s [9] in cohort three) and an sPAP that was not significantly elevated (22 mmHg [23] in cohort one and 34 mmHg [31] in cohort three). The incidence of ACP was low: 2/22 (9%) in cohort one and 3/23 (14%) in cohort three.

Follow-up echocardiography

Follow-up echocardiographic data were available for eight (36%) patients from cohort one. The median time difference between the initial and follow-up scans was 246 (14) days. A comparison of the data and summary statistics is presented in **Table 3**, with individual before-after data in **Figure 3A-D**. All patients with a follow-up echocardiogram had normal RV systolic function, and almost all (7/8, 88%) had normal LV systolic function. The proportion of patients who had RV dilation on their first echocardiogram dropped by half (25% to 13%), and no repeat echocardiograms had features consistent with ACP.

There was no difference in the medians for TAPSE, TRPeakVel, or sPAP across the two-time points. The median pulmonary artery acceleration time (PAAT) increased by ten msec (92 msec to 102 msec), demonstrating a trend to return to what is considered a non-pathological value (i.e., >100 msec) in the previously published literature. (14)

Post-COVID symptom burden (C19-YRS)

Of the 22 patients in cohort one, 21 (95%) were eligible to complete the C19-YRS tool (one patient was blind and non-verbal). 12/22 (55%) completed the questionnaire. Individual patient before-after data for selected domains (overall health, fatigue, breathlessness, and ability to complete activities of daily living) is presented in **Figure 4A-D**.

For overall health pre-illness, the median score was ten (0) compared to eight (2) for post-illness scores (where ten reflects the best possible health). Regarding specific symptom and impairment questions (where zero reflects no symptoms), the median pre/post scores in the breathlessness domain were zero (1) and two (3.5), in the fatigue domain were zero (1) and one (3), and in the ability to complete activities of the daily living domain were zero (0.8) and 0.5 (3).

Severity indices

There was a statistically significant difference between cohorts in markers of disease severity at the time of admission to the ICU, including Sequential Organ Failure Assessment (SOFA, p=0.01), Acute Physiology, Age and Chronic Health Evaluation (APACHE III, p<0.001), and Carrico index (p=0.036). Subgroup comparison to demonstrate where the significant differences lie across the four groups is shown in **Figure 2C-E**.

Troponin was measured in the majority of patients across the cohorts (86%, 79%, 100%, and 100% for cohorts 1-4, respectively). Median peak troponin was highest in cohort three at 145 ng/l (202) (reference range <50 ng/l), followed by cohort one at 62 ng/l (106), cohort four at 44 ng/l (IQR 29), then cohort two at 14 ng/l (65), with a non-significant between-group difference (p=0.45).

Discussion

This data shows no statistically significant difference in any of the measured echocardiographic parameters between survivors and non-survivors in a critically ill COVID-19 population, although there were trends toward worsening parameters of the right ventricle-pulmonary vasculature relationship between the groups. The longitudinal echocardiographic data showed normalisation of the majority of initial echocardiographic abnormalities, with cardiopulmonary symptoms of post-acute COVID syndrome persisting despite echo improvement.

Echocardiographic assessment of the right ventricle in critical COVID-19 disease has demonstrated that dysfunction prevalence varied on the technique with which it was assessed: Price et al. (15) in a cohort of ninety patients demonstrated RV dysfunction using fractional area change (FAC) in 72%, however, if TAPSE was used this fell to 23.8%, echoing the recent multi-centre ECHO-COVID study which showed a median TAPSE in 537 ICU COVID patients of 20.9 mm (interquartile range 17-24). (8) Our data is consistent with these studies, showing normal or near-normal TAPSE across both survivors and non-survivors. COVID-19 has demonstrated that the complex structural and functional adaptations of the RV in response to volume and/or pressure overload are not represented with unidirectional measures such as TAPSE. (15,16)

RV-PA coupling represents an assessment of myocardial shortening relative to generated force and has demonstrable prognostic utility in heart failure, where a lower value (uncoupled) indicates loss of RV contractile ability for a given load and is associated with increased mortality. (17) Using the formula TAPSE/sPAP to assess coupling relies on right ventricular longitudinal shortening to be representative of all components of RV function (i.e., disregards the effect of radial and circumferential shortening on overall systolic function), where a ratio ≥0.65 is normal and ≤0.35 represents severe uncoupling. Although both cohort one (survivors) and cohort three (non-survivors) had median TAPSE within the normal range, it was only cohort 3 that demonstrated uncoupling. Whilst the between-group difference didn't meet statistical significance, this finding illustrates the need to assess the RV-PA complex in its entirety rather than as individual parts.

A stepwise progression in the PAAT can be seen from non-survivors (median 81 msec) to the echo performed in the ICU of survivors (median 92 msec) to the follow-up scan of the survivors (median 102 msec). Acknowledging that the between cohort differences didn't reach statistical significance, we believe this remains a relevant finding of this study, knowing that an accepted cut-off for a short PAAT (reflecting a pulmonary vascular resistance of >3 Woods units) is 90-100 msec in pulmonary hypertension and health, respectively. (18,19)

Indicators of disease severity include the fraction of inspired oxygen (FiO2) requirement at admission to ICU, the ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO2/FiO2), APACHE III score, APACHE III risk of death, SOFA, and peak serum troponin were all higher in cohorts three and four, whilst the SOFA score across all cohorts showed little variability. The lack of SOFA score variability may reflect the primary mechanism of acute severe illness in COVID-19 being 'single-organ' failure, at least in the initial (i.e., admission to ICU) phase, whilst the variables that constitute the SOFA score are multi-domain.

The longitudinal component of this study provides insight into how these patients progress over time. Whilst the number of patients with follow-up studies is small, the individual patient data provides a signal of improvement in echocardiographically appreciable cardiac and cardiopulmonary mechanics. In this context, the persistence of symptoms and impaired overall health perception on the CY19-YRS questionnaire leads to interesting questions that need to be addressed in future research. Whilst post-acute COVID-19 syndrome has a broad range of manifestations and as yet unclear pathophysiology, (20) delineation of the symptom burden attributable to post-COVID from that attributable to the post-ICU syndrome is challenging, with both disease processes needing long-term surveillance. (21) The combination of improving TTE parameters and ongoing symptoms suggests that a cardiac contribu-

tion to symptoms cannot be detected on static assessment - functional testing such as maximal cardiopulmonary exercise testing will likely be of benefit to assess and rehabilitate such patients. (22,23)

Strengths and limitations

There are limitations to this study. It was a single centre with original TTE data acquired retrospectively. TTE was performed as clinically indicated rather than as part of a research protocol, leading to approximately half the cohort not having an echocardiogram performed, thus introducing selection bias. Illness severity and patient comorbidities (i.e., obesity) resulted in limited echocardiographic measures for some patients, so parameters such as FAC could not be determined. Whilst the total number of intubated patients was low, this can affect some TTE indices and was not accounted for here. Pre-existing cardiac dysfunction was not considered in this study, so any underlying cardiac function abnormalities will be a source of error in interpreting the echocardiographic data; however, the median age in cohorts one to three was relatively young. Patient numbers were limited, and not all of cohort one returned for a follow-up echocardiogram, limiting the strength of conclusions that could be drawn.

Additionally, vaccination for COVID-19 commenced during the study period, and by the end of the study period, 18,845,845 Australians over the age of 16 had received two doses. (24) Whilst many available COVID-19 vaccines have demonstrated efficacy in reducing the incidence of severe COVID-19 respiratory illness, (25) their effect on the cardiovascular health of critically ill COVID-19 patients is unclear.

This study also had strengths. It included internationally accepted illness severity scores for a defined cohort of critically ill patients. It included TTE data from survivors and non-survivors, and prospectively acquired longitudinal data adequately demonstrated change over time. Throughout the study period, there were no significant advances in disease treatment, so no therapeutic breakthroughs need to be considered as modifiers to the data presented here.

Conclusion

In summary, we present clinical, echocardiographic, and symptom data on a cohort of patients with COVID-19 requiring ICU admission, demonstrating a trend towards worse outcomes with worsening parameters of right heart function. Reassuringly, perturbed TTE indices typically improve over time, although symptoms persist, highlighting the need for surveillance programs and functional testing for more advanced assessment of these patients.

Interest statement

Declarations of interest: none for all authors. There are no financial declarations for any of the authors. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Table 1. Characteristics of the study population

	Cohort 1 (n=22)	Cohort 2 (n=39)	Cohort 3 (n=23)	Cohort 4 (n=5)	p-value
Age (years)	50 (18.5)	43 (26)	53 (16.5)	72 (10)	0.0024
Gender (male)	16 (73)	21 (54)	15 (65)	3 (60)	0.54
BMI	38.5 (13.7)	32.5 (14.2)	32.6 (13)	28.7 (5.5)	0.11
At least 1 comorbidity - Diabetes mellitus - Immunosuppression - Chronic respiratory disease - Chronic cardiac disease - Chronic renal disease	7 (32) 7 (32) 0 1 (5) 2 (9) 0	15 (38) 9 (21) 0 4 (10) 4 (10) 1 (3)	17 (74) 12 (52) 3 (13) 5 (22) 7 (30) 1 (4)	2 (40) 1 (20) 0 0 2 (40) 0	0.08
ICU length of stay (hours)	151.3 (141.2)	84.4 (120)	213.6 (286.2)	29.7 (65.2)	<0.001
Hospital length of stay (hours)	516 (364.7)	355.9 (215.1)	480.2 (374.4)	164.9 (149.5)	0.0048
Troponin measurement performed - Peak troponin (ng/l)	19 (86) 62 (106)	31 (79) 14 (65)	23 (100) 145 (202)	5 (100) 44 (29)	0.45
SOFA (calculated at admission)[a]	4 (1)	4 (1.5)	5 (2)	5 (2.75)	0.017
% FiO2 at admission	50 (42.5)	50 (20)	80 (12.5)	100 (20)	<0.001
PaO2/FiO2	142 (110)	132 (64)	81 (26)	73 (15)	0.036
APACHE III score	44 (16)	39 (24.5)	55 (21)	79 (35)	<0.001
% APACHE III risk of death	9.9 (9.2)	8.4 (11.8)	20.4 (18.7)	55.1 (31.3)	<0.001
Received invasive ventilation	8 (36)	5 (8)	21 (87)	4 (80)	<0.001
Invasive ventilation time (hours)[b]	156.1 (292.3)	156.9 (59.7)	132.7 (59.7)	21.7 (36.7)	0.069
Received non-invasive ventilation	20 (91)	28 (72)	14 (61)	1 (20%)	0.0086
Non-invasive ventilation time (hours)[c]	28.4 (62.0)	18.7 (37.2)	58.5 (35.4)	0	0.047
Transitioned to ECMO - Survived to ECMO decannulation	0 (0) -	0 (0) -	7 (30.4) 1 (14.3)	0 (0) -	-
Received renal replacement therapy	1 (4.5)	1 (2.6)	3 (13)	1 (20)	0.25
Steroid administration	22 (100)	37 (94.9)	23 (100)	5 (100)	0.41
Remdesivir administration	16 (72.7)	31 (79.5)	21 (91.3)	3 (60)	0.39
Tocilizumab administration	2 (9.1)	8 (20.5)	3 (13)	2 (40)	0.32
Baricitinib administration	14 (59)	15 (38.5)	18 (78.3)	2 (40)	0.015

Legend: Presented as n (%) for categorical data or median (interquartile range) for continuous data. BMI=body mass index; ICU=intensive care unit; SOFA=Sequential Organ Failure Assessment; FiO2=fraction of inspired oxygen; PaO2=arterial oxygen partial pressure; APACHE III=Acute Physiology and Chronic Health Evaluation III; ECMO=extra-corporeal membrane oxygenation.

[a]Missing data means median SOFA scores are calculated with n=21, n=35, n=23, and n=4 patients for cohorts 1-4, respectively; [b]Only includes those who received invasive ventilation; [c]Includes those who received non-invasive ventilation (both continuous positive airway pressure or bilevel positive airway pressure).

Table 2. Echocardiographic comparison between cohort 1 (survivors) and cohort 3 (non-survivors)[a]

	Cohort 1 summary statistic	Cohort 3 summary statistic	Significance
Left ventricular ejection fraction (%)	55 (14.75)	55 (8)	p=0.98
Left ventricular subjective systolic function assessment			p=0.73
- Normal	15/22 (68%)	14/23 (64%)	
- Mild impairment	4/22 (19%)	4/23 (17%)	
- Moderate impairment	2/22 (10%)	2/23 (9%)	
- Severe impairment	1/22 (5%)	1/23 (5%)	
- Hyperdynamic	0/22 (0%)	2/23 (9%)	
Right ventricular subjective systolic function assessment			p=1.0
- Normal	17/21 (81%)	19/23 (83%)	
- Mild impairment	2/21 (10%)	2/23 (9%)	
- Moderate impairment	1/21 (5%)	1/23 (4%)	
- Severe impairment	1/21 (5%)	1/23 (4%)	
Presence of right ventricular dilation	4/20 (20%)	5/23 (22%)	p=0.89
Presence of acute cor pulmonale	2/19 (9%)	3/22 (14%)	p=0.76
TAPSE (cm/sec)	19 (7) (n=21)	21 (9) (n=23)	p=0.32
PAAT (msec)	92 (47) (n=17)	81 (34) (n=21)	p=0.21
TRPeakVel (m/sec)	2.2 (1.3) (n=16)	2.7 (2.0) (n=17)	p=0.15
sPAP (mmHg)	22 (23) (n=15)	34 (31) (n=14)	p=0.17
TAPSE/sPAP	0.98 (1.28) (n=14)	0.59 (2.03) (n=18)	p=0.11
Presence of left atrial dilation	5/21 (24%)	8/21 (38%)	p=0.31
E/e’	7.2 (3.5) (n=19)	8.6 (2.8) (n=21)	p=0.22

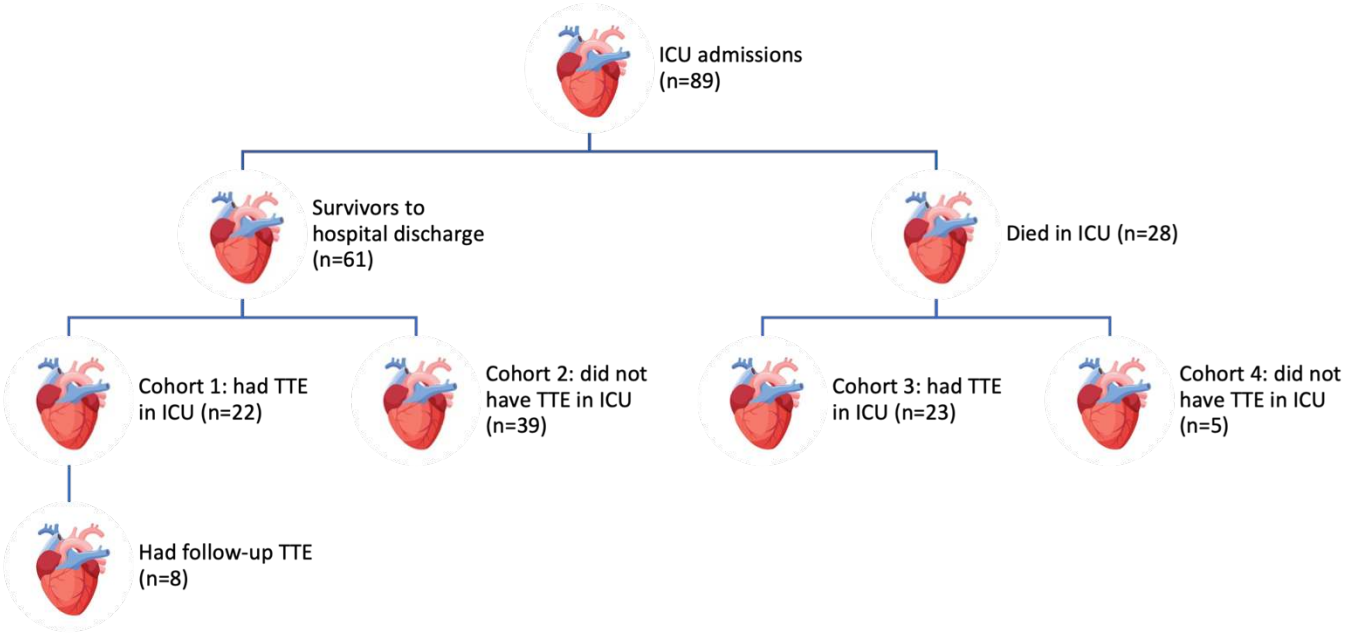
Legend: Presented as n (%) for categorical data or median (interquartile range) for continuous data. TAPSE=tricuspid annular plane systolic excursion; PAAT=pulmonary artery acceleration time; TRPeakVel=peak velocity of the tricuspid regurgitation signal; sPAP=systolic pulmonary artery pressure.
[a] In patients in whom a measure was not technically possible, the number of available measures is listed as either the denominator or n=number.

Table 3. Comparison of echocardiographic parameters for cohort 1 between acute illness (scan 1) and post-discharge (scan 2)[a]

	ICU scan summary statistic	Follow-up scan summary statistic	Significance[b]
Left ventricular ejection fraction (%)	55 (14.75)	55(5)	p=0.67
Left ventricular systolic function assessment			p=0.68
- Normal	15/22 (68%)	7/8 (88%)	
- Mild impairment	4/22 (19%)	1/8 (13%)	
- Moderate impairment	2/22 (10%)	0/8 (0%)	
- Severe impairment	1/22 (5%)	0/8 (0%)	
- Hyperdynamic	0/22 (0%)	0/8 (0%)	
Right ventricular systolic function assessment			p=0.62
- Normal	17/21 (81%)	8/8 (100%)	
- Mild impairment	2/21 (10%)	0/8 (0%)	
- Moderate impairment	1/21 (5%)	0/8 (0%)	
- Severe impairment	1/21 (5%)	0/8 (0%)	
Presence of right ventricular dilation	4/20 (20%)	1/8 (13%)	p=0.37
Presence of acute cor pulmonale	2/19 (9%)	0/8 (0%)	p=0.058
TAPSE (cm/sec)	19 (7) (n=21)	21 (2.5) (n=8)	p=0.73
PAAT (msec)	92 (47) (n=17)	102 (24) (n=8)	p=0.84
TRPeakVel (m/sec)	2.2 (1.3) (n=16)	2.2 (0.3) (n=7)	p=0.44
sPAP (mmHg)	22 (23) (n=15)	22.4 (4.5) (n=7)	p=0.22
TAPSE/sPAP	0.98 (1.28) (n=14)	0.94 (0.28) (n=7)	p=0.97
Presence of left atrial dilation	5/21 (24%)	2/8 (25%)	p=0.16
E/e’	7.2 (3.5) (n=19)	6.4 (1) (n=8)	p=0.047

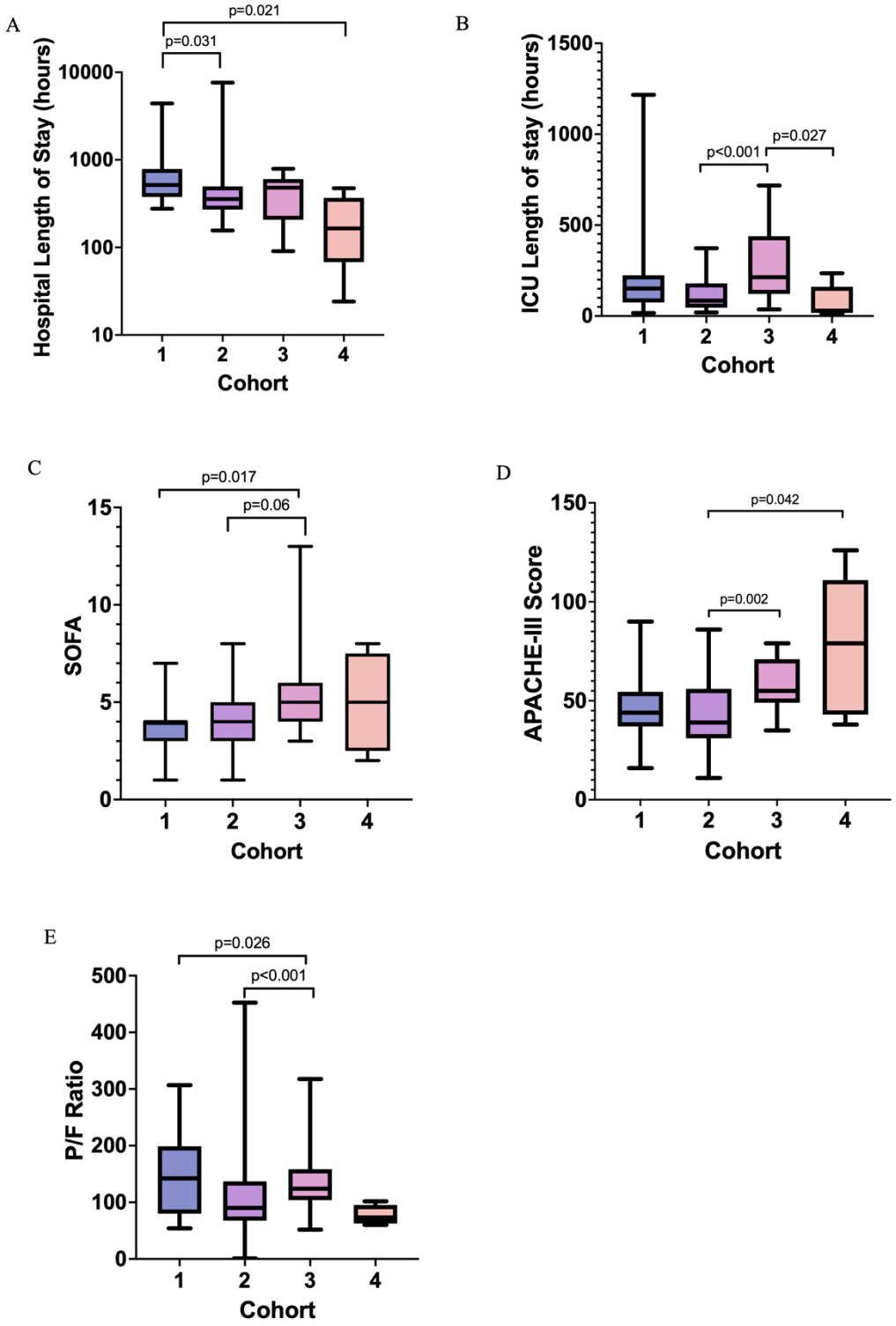
Legend: Presented as n (%) for categorical data or median (interquartile range) for continuous data. TAPSE=tricuspid annular plane systolic excursion; PAAT=pulmonary artery acceleration time; TRPeakVel=peak velocity of the tricuspid regurgitation signal; sPAP=systolic pulmonary artery pressure; ICU=intensive care unit.
[a] In patients in whom a measure was not technically possible, the number of available measures is listed as either the denominator or n=number.
[b] Categorical data analysed as binary data (normal/abnormal).

Figure 1. Cohort diagram



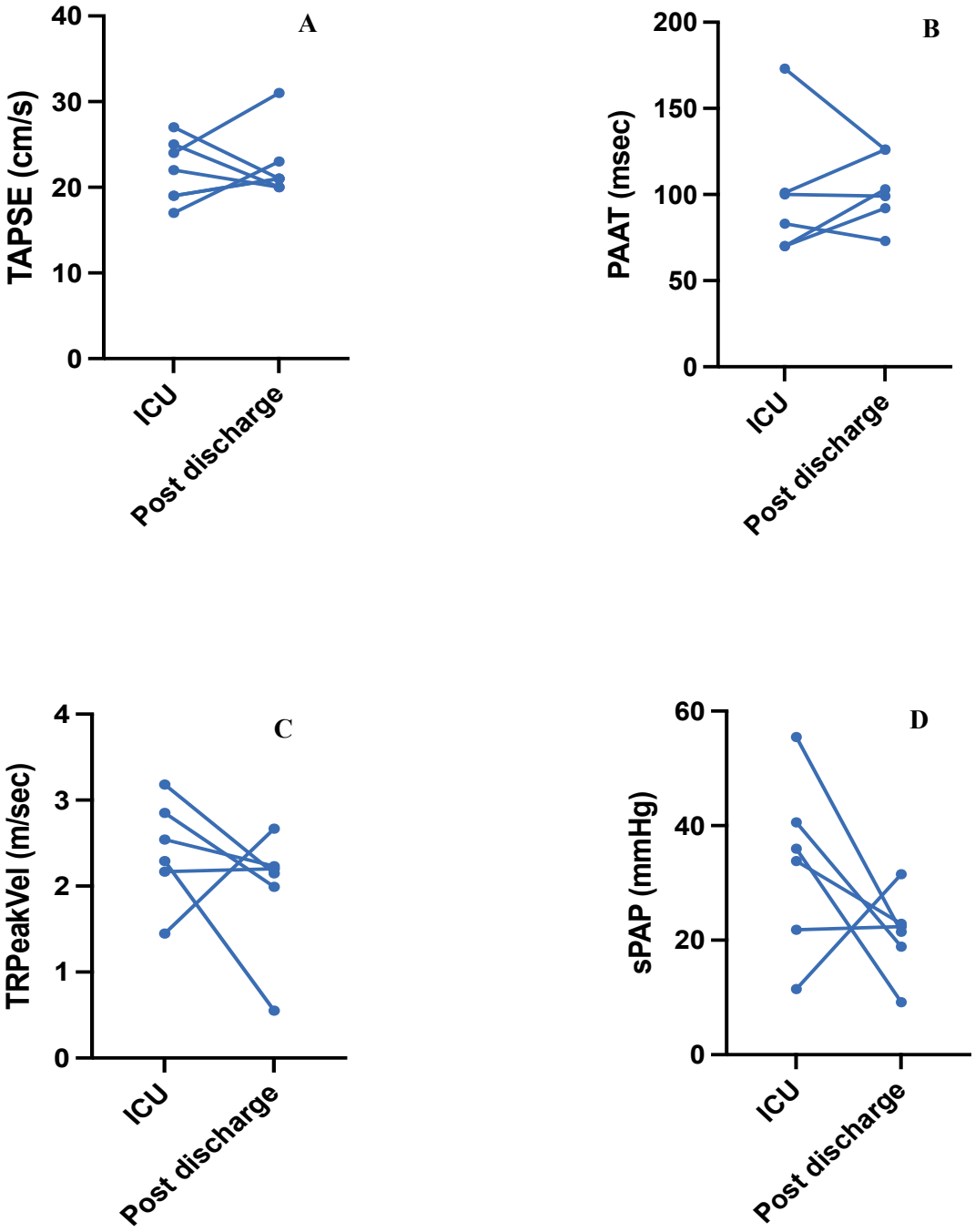
Legend: ICU=intensive care unit; TTE=transthoracic echocardiogram.

Figures 2A-E. Comparison of length of stay and severity indices between cohorts



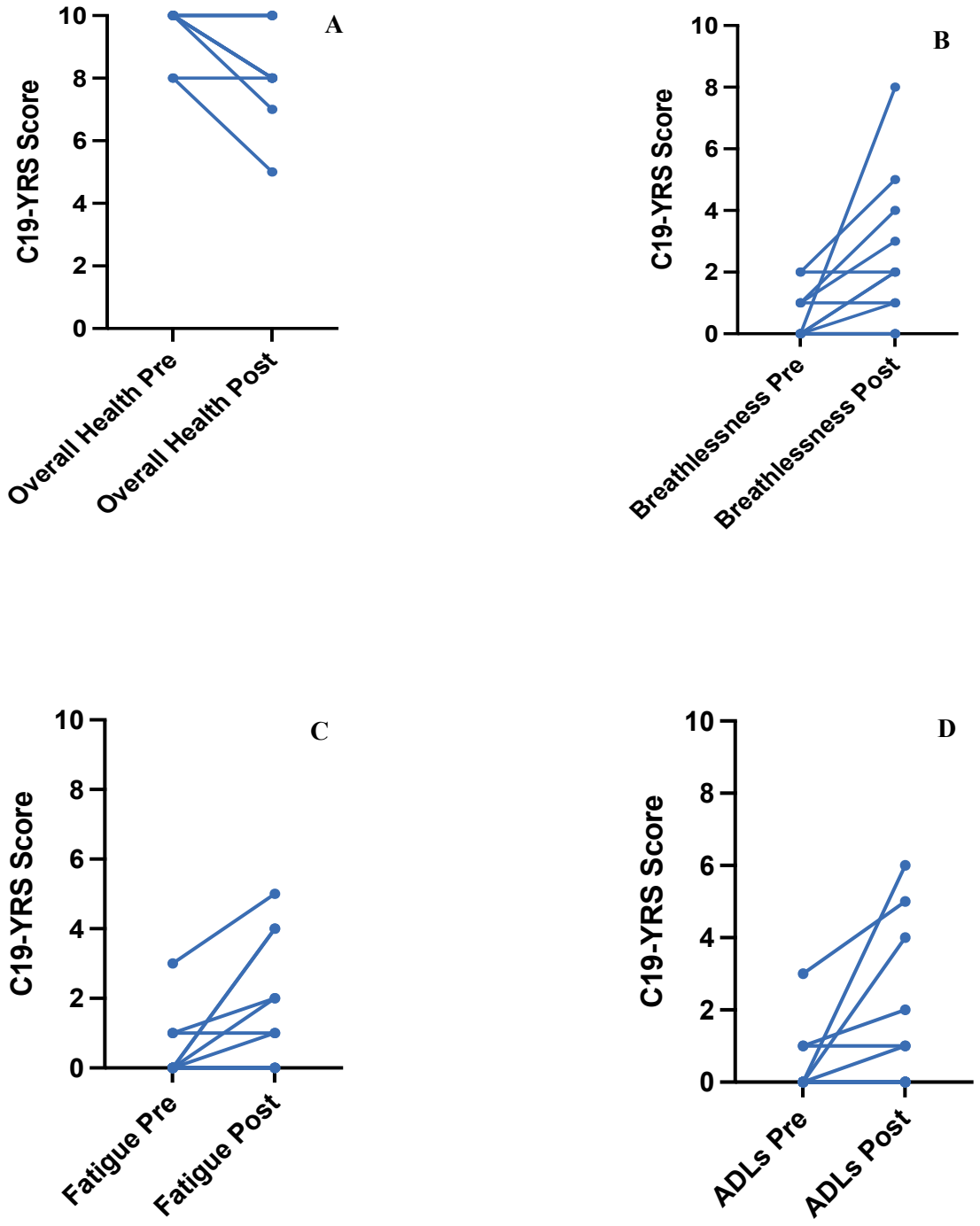
Legend: ICU=intensive care unit; SOFA=Sequential Organ Failure Assessment; APACHE III=Acute Physiology and Chronic Health Evaluation III; P/F=PaO2 (arterial oxygen partial pressure)/FiO2 (fraction of inspired oxygen).
Length of stay and selected severity indices show the significance between cohort differences. Unmarked pairwise comparisons are not significant.

Figures 3A-D. Change of RV indices between ICU and post-discharge



Legend: RV=right ventricular; ICU=intensive care unit; TAPSE=tricuspid annular plane systolic excursion; ICU=intensive care unit; PAAT=pulmonary artery acceleration time; TRPeakVel=peak velocity of the tricuspid regurgitation signal; sPAP=systolic pulmonary artery pressure.
Before-after plots showing individual patient data points for echocardiographic parameters measured during acute COVID-19 infection ("ICU") and on follow-up echocardiogram ("Post discharge") for TAPSE (A), PAAT (B), TRPeakVel (C), and sPAP (D).

Figures 4A-D. C19-YRS selected domains for survivors



Legend: C19-YRS=coronavirus disease 2019 (COVID-19) Yorkshire Rehabilitation Scale; ADLs=activities of daily living.
Individual patient before-after data for 4 selected domains of the C19-YRS tool: overall health (A), breathlessness (B), overall fatigue (C), and ability to complete activities of daily living (D). Note: for A, ten represents the best overall health with no limitations, whereas, for B, C, and D, zero represents no symptoms/limitations.

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