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## **Usefulness of right ventricular longitudinal shortening fraction to detect right ventricular dysfunction in acute cor pulmonale related to COVID-19.**

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**Brief title:** Acute cor pulmonale in COVID-19

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## Introduction

Right ventricular (RV) dysfunction evaluated by echocardiography is a non-rare complication of COVID-19 infection, with an estimated incidence of 27%[1]. RV systolic function is classically assessed with transthoracic echocardiography (TTE) by RV-fractional area change (RV-FAC), tricuspid annular plane systolic excursion (TAPSE) or S' tricuspid systolic (RV-S') wave velocity obtained by tissue-Doppler imaging [2]. More recently, two-dimensional speckle tracking echocardiography (2D-STE), a semi-automated angle independent method, has been developed to evaluate the RV systolic function [2–4]. RV free wall longitudinal strain (RVFWLS), a 2D-STE parameter, seems to be a good predictor of mortality in COVID-19 patients [5]. However, there are limited data regarding the use of RVFWLS in acute respiratory distress syndrome (ARDS) related to COVID-19 (CARDS), especially in the presence of an acute cor pulmonale (ACP), a well-known and deadly complication of ARDS under mechanical ventilation[6]. ACP related to ARDS is characterized by RV dilatation associated with modifications in RV chamber geometry and with myocardial mechanical dyssynchrony (septal dyskinesia). These factors are known to have significant impact on strain values[4].

Recently, a relatively new 2D-STE parameter based on tricuspid annular longitudinal displacement (TAD) has been proposed to evaluate RV systolic function[7, 8]: the RV longitudinal shortening fraction (RV-LSF). Like TMAD (tissue mitral annular displacement) that estimates the ejection fraction of the left ventricle via 2D-STE [9], RV-LSF assesses the global systolic function of the RV by calculating the shortening of the tricuspid annulus towards the RV using 2D-STE. To the contrary to TAPSE, an M-mode parameter, that analyses the RV longitudinal function only in one dimension [2], RV-LSF is an angle-independent, automatically calculated and reproducible parameter which is less dependent on

image quality than strain parameters such as RVFWLS or RV global longitudinal strain (RVGLS) [10] . For patients with ACP, the main advantage of RV-LSF compared to other 2D-STE parameters is to **be less effected** by RV geometry or by myocardial dyskinesia [4].

The aim of this study was to compare the diagnostic ability of different 2D-STE parameters with that of conventional echocardiographic parameters to detect RV systolic dysfunction in mechanically ventilated CARDS patients with and without ACP. **Our hypothesis is that the RV-LSF could identify RV dysfunction accurately in patients with ACP. This hypothesis was tested using RV-FAC, measured by TEE, as a reference method for RV dysfunction evaluation [2] [3].**

## **Material and Methods**

### **Population**

Adult patients (>18 years of age) admitted to our intensive care unit (ICU) for moderate to severe ARDS under mechanical ventilation, related to SARS-Cov2 infection were prospectively included in the study. Exclusion criteria were permanent ventricular pacing, previous known RV systolic ventricular dysfunction, contra-indications to transoesophageal echocardiography (TEE) (esophageal disease or major uncontrolled bleeding) and patients under extracorporeal membrane oxygenation (ECMO).

This study was approved by the Amiens University Hospital IRB (Comite de Protection des Personnes Nord-Ouest II CHU–Place V. Pauchet, 80054 AMIENS Cedex 1, CNIL Number: PI2020\_843\_0026). In accordance with French law on clinical research for non-interventional studies, informed consent was waived but oral and written information was provided whenever possible to the patients and systematically to their families specifying that they could oppose the use of their data [11].

Data from electronic data and medical reports were collected prospectively. SARS-Cov2 infection was confirmed by a positive rT-PCR on nasopharyngeal swab or bronchoalveolar lavage on admission to our critical care unit. The ARDS grade was defined according to the Berlin definition[12]. The severity of illness upon ICU admission was evaluated by the sepsis-related organ failure assessment score (SOFA score) [13]. Chest computed tomography angiogram was performed prior to tracheal intubation to diagnose pulmonary embolism.

TTE and TEE were performed simultaneously, for all patients in supine position, within 24 hours of tracheal intubation, by trained operators using a standardized procedure. Some parameters were assessed by TTE and other by TEE. Indeed, TTE is better for the assessment of conventional RV parameters whilst TEE is known to significantly underestimate TAPSE and RV-S' wave velocity [14]. TEE was used for 2D-STE parameters evaluation because image quality obtained by TTE was usually not sufficient to accurately measure 2D-STE parameters. Moreover, in mechanically ventilated patients, it is often difficult to obtain an apical four-chamber view focused on the RV as recommended [15]. During the echocardiography examination, all patients were sedated and paralyzed in accordance with ARDS guidelines management [16]. In our center, TTE and TEE are performed routinely for ARDS patients in order to manage ventilator settings, fluid responsiveness and to assess RV and LV systolic function [17]. In ARDS patient, we use TEE to more accurately diagnose ACP and to analyze the interatrial septum in search for intracardiac shunt [18] [19]. All echocardiographic images were analyzed offline.

## **Echocardiography**

### ***TTE measurement***

*RV systolic function analysis* : **Conventional** RV parameters (TAPSE, RV-S' and RV-FAC) were measured, according to international guidelines [2]:

**TAPSE was measured** using M-mode **with cursor placed at the junction of the lateral tricuspid leaflet and the RV free wall. RV-S' wave was measured** in the apical four chamber view **using Doppler tissue imaging mode. RV systolic and diastolic areas were measured** in the apical four chamber view in 2D mode. RV-FAC was calculated by subtracting the end-systolic area from the end-diastolic area and dividing this value by the end-diastolic area. **Basal, mid-cavity and longitudinal linear dimensions were measured in a RV focused apical**

**four chamber.** RV systolic dysfunction was defined as RV-FAC <35% as recommended by the American Society of Echocardiography and the European Association of Cardiovascular Imaging [3]. **Distal RV outflow tract (RVOT) diameter was measured in a para-sternal short axis view. In the same view, RVOT velocity time integral (RVOT VTI) and RVOT acceleration time (AT<sub>RVOT</sub>) were obtained from the RVOT pulse wave Doppler profile. RA volume was measured on the apical four -chamber view with 2D volumetric measurement based on tracings of the blood tissue interface.** RA volume, RV area and RV stroke volume were indexed to the body surface area.

*RV hemodynamic:* RA pressure was estimated, in TTE, by the examination of the diameter of the inferior vena cava from the subcostal view and the percentage decrease in the diameter during respiratory cycle [3]. RV stroke volume (RV SV) was calculated non-invasively as follow:  $RV\ SV = (RVOT\ VTI) \times \pi \times (RVOT\ diameter)^2 / 4$ . [20].

### ***TEE measurement***

*Diagnostic of ACP:* In the four-chamber view at the mid-esophageal level (ME 4CH) (**Video 1**), RV end-diastolic area to left ventricular end-diastolic area were measured and septal motion was carefully observed. ACP was defined as the ratio of RV end-diastolic area to left ventricular end-diastolic area >0.6 associated with septal dyskinesia [6].

*Speckle tracking Analysis:* RV strain measured by speckle-tracking echocardiography was obtained using a dedicated software (Automated Cardiac Motion Quantification, QLAB version 9.0, Philips Medical systems, Andover, MA, USA). **All 2D-STE measurements were performed by a cardiologist experienced in echocardiography.** 2D-STE parameters were

analysed in single frame and the reported values were the average of 3 measurements. 2D-STE parameters were obtained by TEE **in the ME 4CH view**.

*Tricuspid annular displacement analysis:* For TAD analysis, three points were used for initialization on the first diastolic frame in 2D ME 4CH view (**Image 1A**). These points were placed 1) on the tricuspid annulus, at the insertion of the anterior tricuspid valve leaflet (RV free wall), 2) on the tricuspid annulus, at the insertion of the septal leaflet and 3) on the RV apex. The software (**Automated Cardiac Motion Quantification, QLAB version 9.0, Philips Medical systems, Andover, MA, USA**) automatically tracked and calculated 3 parameters: (1) the displacement between the RV free wall and the RV apex ( $TAD_{lat}$ ), (2) the displacement between the interventricular septum and the RV apex ( $TAD_{sep}$ ) and (3) the RV-LSF. RV-LSF was calculated as the maximum end-systolic displacement (LES) of the mid-annular point from the measured annular motion and is expressed in percent of the end diastolic RV longitudinal dimension (LED):  $100 \times (LED - LES)/LED$ . The mid-annular point was automatically selected by the software (**Video 2**).

*2D-strain analysis:* The left ventricle specific strain software was used for RV strain analysis as RV specific software was not available. The region of interests (ROI) were generated automatically and adjusted manually whenever the automated ROI were of poor quality. A full wall approach was used for RV strain analysis **in a 2D ME 4CH view**: endocardial border of the RV was manually traced at end systole and automatically adjusted to include the entire myocardium. RVFWLS was calculated as the average of the three segments (**Figure 1B**). For RVGLS, 6 segments were analysed (**Figure 1C**). Segments for which adequate tracking quality was not obtained despite manual adjustment were excluded from the analysis. Longitudinal strain was defined as the percentage of myocardial shortening relative to the

original length and presented as a negative value: a more negative strain value reflecting better shortening [2].

### **Statistical analysis**

Data are expressed as mean  $\pm$  standard deviation (SD), median [interquartile range] or numbers (percentage), as appropriate. ACP group and non-ACP group variables were compared using Mann-Whitney or Chi-square tests, as appropriate. In a second analysis, we compared patients with and patients without RV dysfunction (defined by the RV-FAC<35%). A receiver-operating characteristic curve (ROC) was built to assess the diagnostic performance of 2D-STE parameters, TAPSE and RV-S' wave for RV systolic dysfunction (RV-FAC<35%) in the general population and in the ACP group. Area under ROC curves (AUC) of echocardiographic parameters were compared using Delong's test. Correlations between 2D-STE parameters and RV FAC were assessed using the non-parametric Pearson correlation test in each group (ACP and non-ACP). To assess intra-operator and inter-operator reproducibility for offline analysis, data of 10 patients were randomly selected and analyzed by the same operator and by another operator with an interval of at least one week between the two analyses. The reproducibility of 2D-STE measurements was evaluated using the intraclass correlation coefficient (ICC). All statistical analyses were performed with IBM SPSS software (SPSS, version 24, IBM, New York, NY). The limit of statistical significance was  $P < 0.05$ . All P values are the results of 2-tailed tests.

## Results

Between March 1<sup>st</sup> and April 15<sup>th</sup>, 2020, 84 patients were admitted in our ICU for COVID-19 infection. Among the 54 patients who required mechanical ventilation, 47 patients had moderate to severe ARDS and 29 patients (61%) were included (**Figure 2**). The 2D-STE parameters were feasible for the 29 patients. In 2D-strain analysis no myocardial segments were excluded. Demographic and echocardiographic data are summarized in **Table 1**. Patients were divided in 2 groups according to the presence or the absence of ACP diagnosed by TEE. ACP was diagnosed in 12/29 (41%) patients and was absent in 17/29 (59%). Age, sex, body mass index and all ventilatory parameters were comparable (all  $p \geq 0.11$ ) between the 2 groups. Before tracheal intubation, 26 CT were performed, and pulmonary embolism was diagnosed for 2 patients. There was no significant difference in RV-FAC, S' wave and TAPSE between the 2 groups (ACP versus non-ACP). There was more RV dysfunction in the ACP group than the non-ACP group (n=7/12 vs n=3/17;  $p=0.03$ ).

### **Difference between 2D-STE parameters and conventional parameters in ACP group vs non-ACP group**

2D-STE parameters (RV-LSF and RVFWLS) were markedly altered in the ACP group compared to the non-ACP group (Table1). For conventional RV parameters (TAPSE, RV-S' and RV-FAC), no difference was found between the ACP and non-ACP group.

### TAD parameters

In the ACP group, median RV-LSF was 17 [14-22] % and had the best correlation with RV-FAC ( $r= 0.79$ ,  $p<0.001$  vs.  $r=0.27$ ,  $p=0.39$  for RVGLS and  $r=0.28$ ,  $p=0.39$  for RVFWLS) (**Figure 3A, 3B and 3C**). In the non-ACP group, RV-LSF had the highest correlation ( $r=0.69$ ,  $p<0.002$ ) with RV-FAC (**Figure 3D, 3E, 3F**). The median value of TAPSE and TAD<sub>lat</sub> were closed to each other but linear correlation was not significant. (**Appendix 1**).

### RV Hemodynamics

For RV hemodynamics parameters, no difference was found for RV stroke volume index (32 [27-40] ml.m<sup>-2</sup> vs 33 [27-35] ml.m<sup>-2</sup>,  $p=0.94$ ), RA volume index (19 [16-29] ml.m<sup>-2</sup> vs 19 [15-22] ml.m<sup>-2</sup>,  $p=0.85$ ) and AT<sub>RVOT</sub> (95 [82-145] ms vs 90 [80-120] ms,  $p=0.72$ ) between the ACP group and the non ACP group. **Pulmonary arterial systolic pressure could not be evaluated because more than 70% of the patients had poor quality of the tricuspid regurgitation doppler flow.**

### RV dysfunction versus no RV dysfunction

Ten out of 29 patients (34%) had RV dysfunction (defined by RV-FAC<35%). RV-LSF (15 [11-20] % vs 25 [21-29] %;  $p=0.002$ ) and TAD<sub>lat</sub> (13 [11-20] mm vs 21 [16-28] mm,  $p=0.008$ ) were significantly decreased in the RV dysfunction group. No difference was found between the 2 groups for 2D-strain parameters, TAPSE (22 [20-25] mm vs 24 [21-26] mm;  $p=0.28$ ) and RV-S' (14 [13-19] cm.s<sup>-1</sup> vs 18 [13-20] cm.s<sup>-1</sup>;  $p=0.77$ ) (**Appendix 2**).

### ROC curve analysis

Comparison of ROC curve analysis (**Figure 4**) showed that RV-LSF had the highest AUC to identify RV systolic dysfunction compared to others 2D-STE parameters and to conventional RV systolic parameters in the overall population (**Figure 4A**) and in the ACP group (**Figure 4B**). In the overall population, a RV-LSF cut-off value of 20% had a sensitivity of 84% (IC95% [49.7-96.7]) and a specificity of 90% (IC95% [60.4-99.7]), with an AUC of 0.879 ( $p < 0,001$ , IC95% [0.70-1.00]) to identify RV systolic dysfunction. In the ACP group, a RV-LSF cut-off value of 17 % had a sensitivity of 80% (IC95% [48.7-99.6] and a specificity 86% (IC95% [49.1-99.4], with an AUC of 0.93 ( $p < 0,015$ , IC95% [0.78-1.00]) to identify RV systolic dysfunction (**Figure 4B**).

### **Reproducibility analysis**

The reproducibility of RV-LSF was excellent with an ICC of 0.93 (IC95% 0.74-0.98) for the inter-operator reproducibility and an ICC of 0.96 (IC95% 0.72-0.98) for the intra-operator reproducibility (**Table 2**).

## Discussion

In the setting of COVID-19 patients complicated with ARDS, our results showed that RV dysfunction and ACP are frequent complications (34% and 41% in our series respectively) despite protective ventilation. For patients with CARDS and ACP, our results suggest that (1) 2D-STE parameters (especially RV-LSF) seems to **be more accurate** for RV systolic dysfunction detection than TAPSE or RV-S' wave (2) RV-LSF is well correlated with RV-FAC to the contrary to TAPSE and RV'S wave and 2D-STE parameters (3) RV-LSF might be **a reliable** predictor of RV dysfunction, as TAPSE and S' remained in the normal range.

### *ACP, RV dysfunction and CARDS*

In non-COVID-19 moderate to severe ARDS under mechanical ventilation, the prevalence of ACP (monitored with TEE) was 22%, associated with poor outcome [6] and the prevalence of RV dysfunction varies across studies , ranging from 22% to 50% [21]. The pathophysiology of RV dysfunction in COVID-19 infections remains unknown. RV dysfunction can be due to direct viral effect on heart, pro-inflammatory status, severe hypoxemia or coronary endothelial dysfunction leading to heart failure reflecting the severity of COVID-19 infection [5, 22, 23]. In addition, vascular derangements related to COVID-19 pneumoniae [24] may increase RV preload and afterload at an early stage of the infection, inducing ACP. In a recent prospective international study, Dweck et al. shown that 33 % of COVID-19 patients **have RV abnormalities in TTE** (RV dilatation, RV impairment, D-shape LV and elevated pulmonary artery pressure) and that these abnormalities are more common in patients with severe symptoms of COVID-19 [25]. In this study, 15 % of patients had RV dilatation, but no data on specific RV systolic parameters were reported. In addition, the

proportion of patients with CARDS under mechanical ventilation and the number of patients with ACP were not reported. [24]

In another TTE study, Li et al. demonstrated that RV systolic dysfunction assessed by RVFWLS is a powerful predictor of mortality in male patients with CARDS[5]. In this study, conventional RV systolic parameters (RV FAC, TAPSE and S' wave) in patients of the lower tertile of RVFWLS (<-20.5%) were within normal range. However, only 12.5% (n=15/120) of patients were under mechanical ventilation and proportion of ACP was not reported [5].

### ***RV-LSF and 2D-STE parameters***

In our study, 2D-STE parameters were impaired, unlike conventional RV systolic parameters which remained within normal range. Moreover, we found that RV-LSF in the ACP group, was well correlated with RV-FAC to the contrary to strain parameters, TAPSE and RV S' wave. These results are in accordance with previous studies. Ahmad et al. [26] evaluated the correlation between RV-LSF and RV systolic ejection fraction assessed by cardiac magnetic resonance (CMR-RVEF) in stable patients with RV dysfunction. They found that RV-LSF was more correlated with CMR-RVEF than TAPSE or others speckle tracking parameters [26]. Li et al. [27] showed that RV-LSF has a good correlation with CMR-RVEF in patients with pulmonary hypertension. In this study, the ROC curves analysis demonstrated that RV-LSF could be used to predict RV dysfunction (as assessed by CMR) and that RV-LSF had the higher AUC (0.975 IC95% [0.84-1.00]) compared to TAPSE, RV-FAC and RV-S'wave. [27]. Maniwa et al. investigated the value of RV-LSF for the assessment of RV systolic dysfunction (defined by RV ejection fraction <45% by 3-dimensional TTE) in 61 patients [10]. In their study, RV-LSF had the highest diagnostic accuracy for RV systolic dysfunction, better than TAPSE, RV FAC and RVFWLS. The

feasibility of RV LSF was 91.8 % (n=56/61) and 82 % (n=50/61) for RVFWLS in this report[10].

In conclusion, these studies shown that RV-LSF measurement diagnoses more accurately RV dysfunction than TAPSE or RV-S' wave.

### ***RV-LSF and RV systolic function***

The superiority of RV-LSF over other parameters to identify RV systolic dysfunction can be explained by physiological mechanisms involved in RV contraction and by the clinical significance of this measure. First, RV-LSF allow evaluation of two mechanisms contributing to RV systolic function : (1) the shortening of the longitudinal axis with traction of the tricuspid annulus towards the apex, and (2) (via the septal point) the shortening of the interventricular septum in the anteroposterior direction during left ventricular contraction [28]. Conversely, longitudinal strain incorporate only one motion direction [15]. Under physiological conditions, longitudinal shortening provides a fairly reliable assessment of RV systolic function; which explains the routine clinical use of TAPSE. However, recent studies suggest a similar importance of longitudinal and radial RV motions [28]. In addition to this, ACP is characterized by pressure overload, changes in chamber geometry and desynchronization of myocardial contraction. These factors are known to influence myocardial strain in experimental and mathematical models[4]. Therefore, abnormal strain values may reflect RV physiological adaptation to loading conditions and thus may not be synonymous of myocardial disease. In the other hand, normal values do not exclude disease state [4]. Furthermore, unlike TAPSE and RV-S' wave, the absolute value of RV-LSF is related to RV volume. Hence, RV-LSF is likely to be more correlated to indices using RV volumes as RV-FAC or CMR-EF [26, 27]. Early diagnosis of RV dysfunction is part of the

comprehensive management and treatment of CARDS under mechanical ventilation in order to avoid the development or worsening of ACP and thus hemodynamic deterioration. Besides, RV 2D-STE parameters can be used to evaluate the effectiveness of specific treatments, such as almitrine [29] or to monitor RV systolic function during prone positioning [8].

### ***TAPSE and 2D-STE parameters***

To the contrary to other studies, we found no correlation between TAPSE and  $TAD_{lat}$  [14, 30]. However, these studies assessed  $TAD_{lat}$  and  $TAD_{sep}$  parameters and conventional RV systolic parameters by TEE for patients in the operating theatre during surgery with different hemodynamic and ventilatory conditions than patients with ARDS[30]. One of the major limitation of TAPSE is its large overlap between patients with and without RV dysfunction [31]. Focusing on patients with ARDS, Lemarié et al. used the widely accepted cut-off value of TAPSE ( $TAPSE < 17\text{mm}$ ) and found no difference in survival [32]. Moreover, TAPSE evaluates only the motion of the tricuspid annulus without taking into account the complete longitudinal contraction (from base to apex) as RV-LSF does. Moreover, in ICU, TTE image quality is often impaired by pulmonary disease, mechanical ventilation and suboptimal patient positioning [33].

### ***Reliability***

In our study, measurement of 2D-STE parameters showed a high degree of reliability. The intra and inter observer ICC for RV-LSF were excellent (both  $>0.93$ ) in accordance with previous studies[27].

## **Limitation**

The first limitation of our study is the limited sample size especially in the ACP group. Besides, the absence of difference for TAPSE, RV-S' wave, RV-FAC among ACP and non-ACP patients might be related to the relatively small size of our population. To the contrary to TAPSE and RV-S' wave, 2D-STE parameters, especially RV-LSF, appears to be powerful predictors of RV dysfunction as they differ markedly between the 2 groups even for this limited sample size. Secondly, the sensitivity and specificity values for RV-LSF measurement were calculated by applying the ROC cut-off values and need independent confirmation in prospective studies. In addition, the image quality in ARDS patients can impact the ability to measure RV-FAC [34] and thus affect linear correlation between 2D-STE parameters and RV-FAC. For RV dysfunction evaluation, the three dimensional echocardiographic assessment of RV function has a better correlation with RV ejection fraction calculated by cardiac magnetic resonance than RV-FAC [3]. However, its routine use for bedside assessment remains very limited, especially due to specific probes availability. The left ventricle specific strain software (QLAB version 9.0, Philips Medical systems, Andover, MA, USA) was used for RV strain analysis as RV specific software was not available. Nevertheless, these 2 methods correlate very well even if there are not totally interchangeable [35]. However, despite widespread variability in RV regional strain analysis between vendor software (GE and Philipps), differences do not seem to be significant [36]. Finally, further studies are required to compare ACP and RV dysfunction prevalence according to ARDS etiology (i.e. influenzae, COVID-19, bacterial infection).

**Conclusion**

In CARDS with ACP, RV-LSF seems to be an accurate, reliable and reproducible 2D-STE parameter for evaluating right ventricular systolic function. Further studies with larger sample size investigating outcome related to ACP with RV dysfunction in COVID-19 patients are required.

**Authors' contributions**

Concept and design: CB, OAA, YM

Data Acquisition, analysis, and interpretation: CB, YB, CD, TB

Drafting of the manuscript: CB, YB, YM

Critical revision of the manuscript for important intellectual content: CB, YM, PH.

Statistical analysis: YB, OAA

Supervision: YM

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## Legend of figures

**Figure 1:** Measurement of 2D-STE parameters in a mid-esophageal four-chamber view.

**A. TAD.** A lateral point (blue circle) and a septal point (orange circle) were placed at the bottom of the RV free wall and at the bottom of the interventricular septum. A third point was placed at the apex (yellow circle). TAD lateral, TAD septal and RV longitudinal shortening fraction (%) value were automatically displayed. The mid-annular point is automated selected by the software.

**B. RV global longitudinal strain.** Region of interest were generated automatically and adjusted manually. RV was divided into six segments. RVGLS (%) was calculated as the average of the six segments.

**C. RV free wall longitudinal strain.** Region of interest were generated automatically and adjusted manually. RV was divided into 3 segments and RVFWLS (%) was calculated as the average of the 3 segments

**2D-STE:** bi-dimensionnal speckle tracking echocardiography; **TAD:** tricuspid annular displacement; **RV:** right ventricle; **RVFWLS:** right ventricle free wall longitudinal strain; **RVGLS:** right ventricle global longitudinal strain.

**Figure 2:** Flow diagram of the study group

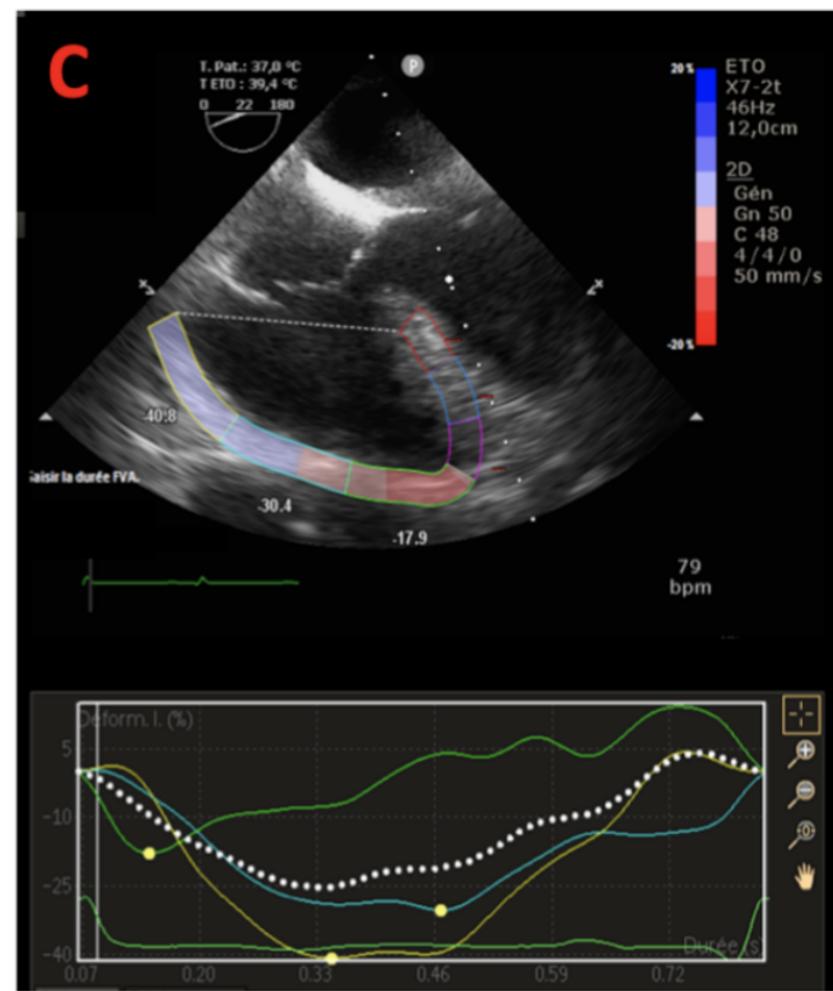
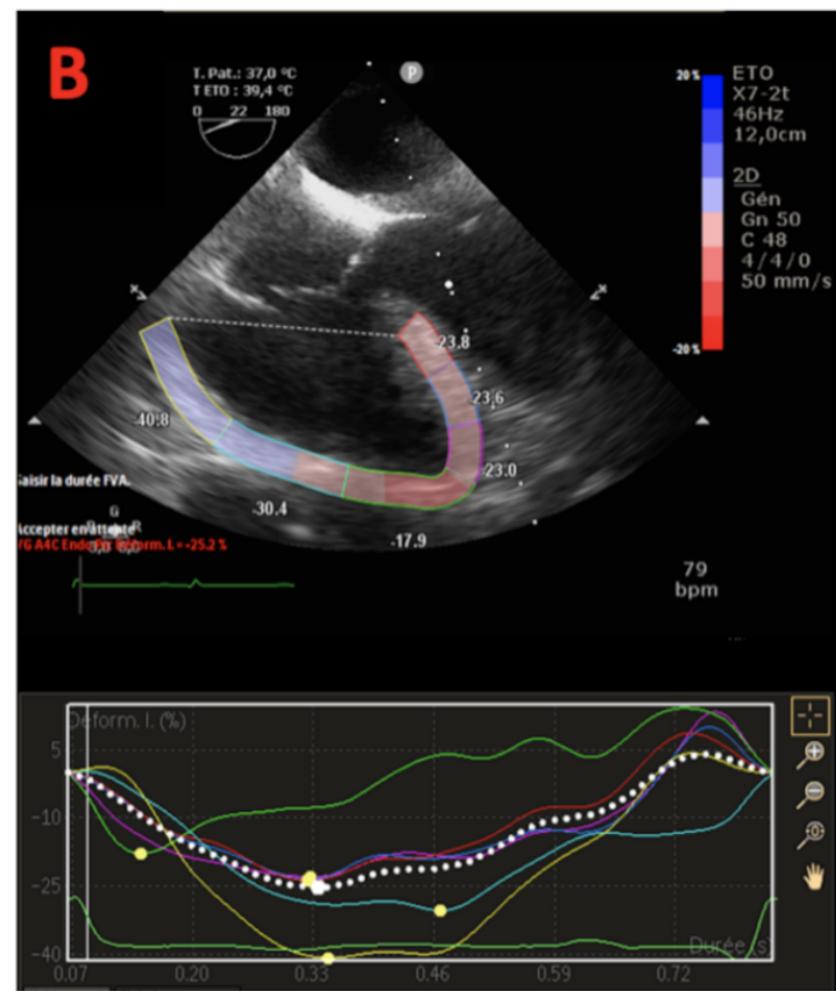
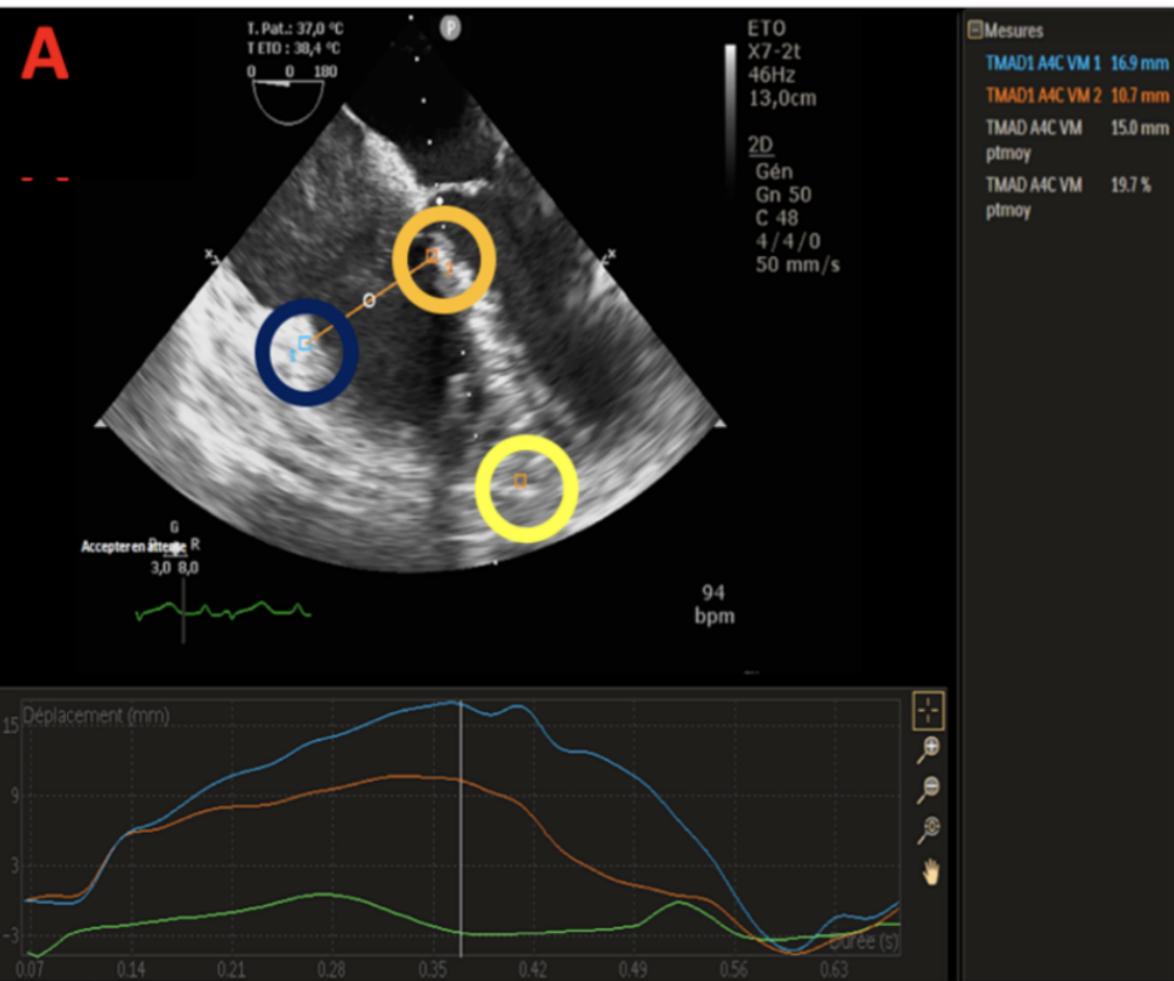
**ARDS:** acute respiratory distress syndrome; **ECMO:** extracorporeal membrane oxygenation; **TEE:** transoesophageal echocardiography.

**Figure 3:** Linear correlation between 2D-STE parameters and RV-FAC in ACP group and non-ACP group

**ACP:** acute cor pulmonale; **2D-STE:** bi-dimensionnal speckle tracking echocardiography; **RV-FAC:** right ventricle fractional area change.

**Figure 4:** ROC curve analysis between 2D-STE parameters and conventional parameters in overall population (A) and ACP group (B).

**ACP:** acute cor pulmonale; **2D-STE:** bi-dimensionnal speckle tracking echocardiography; **ROC:** receiver operating characteristic.



84 patients hospitalized in ICU with pneumonia related to COVID-19 infection between March, 1<sup>st</sup> 2020 and April, 15<sup>th</sup>, 2020

30 patients under non-invasive ventilation

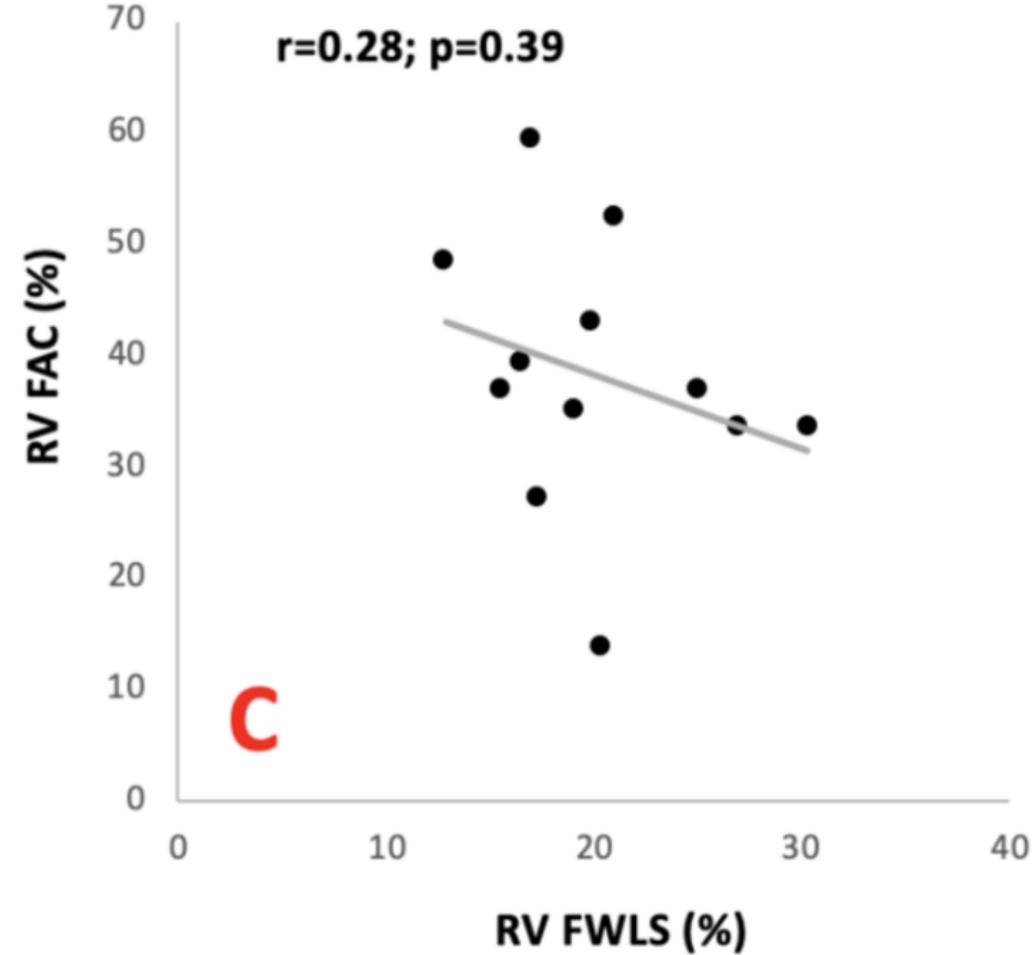
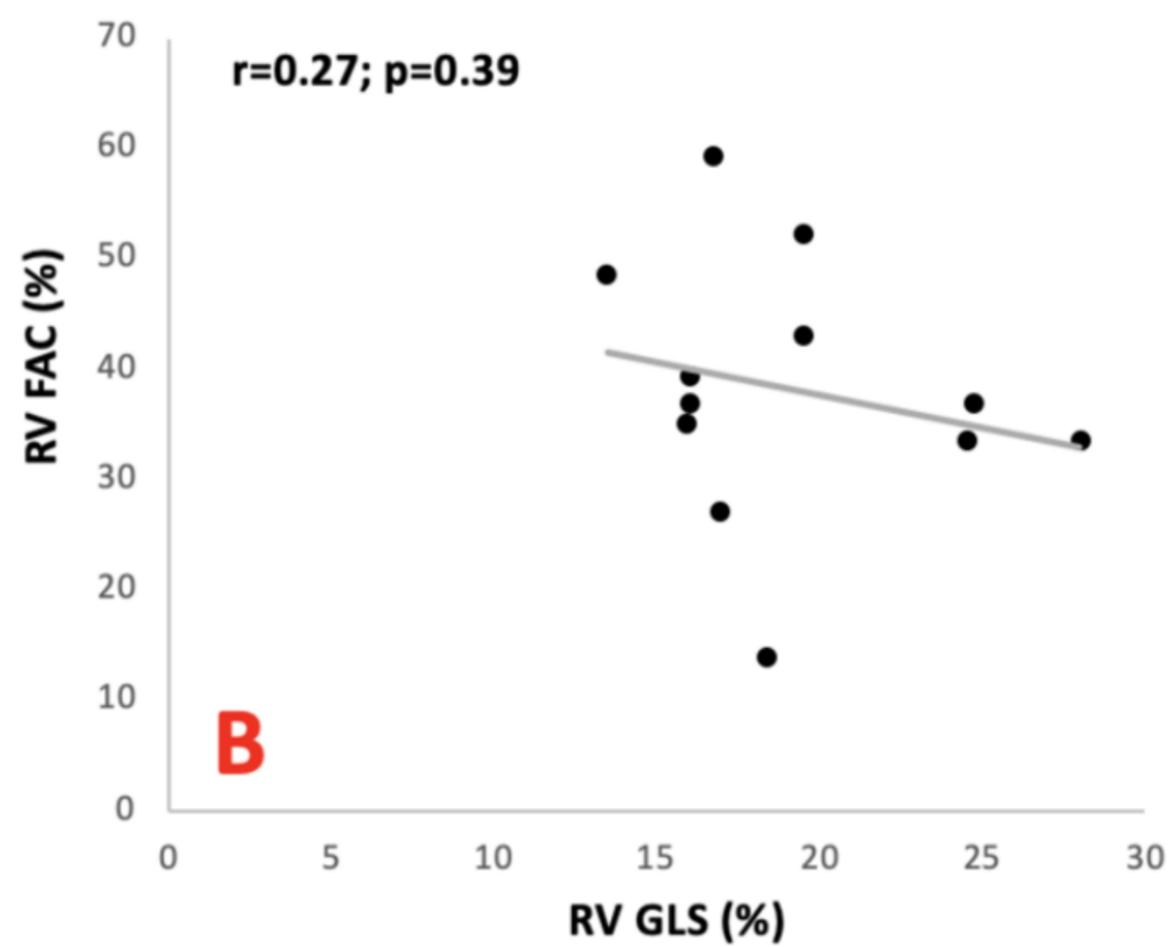
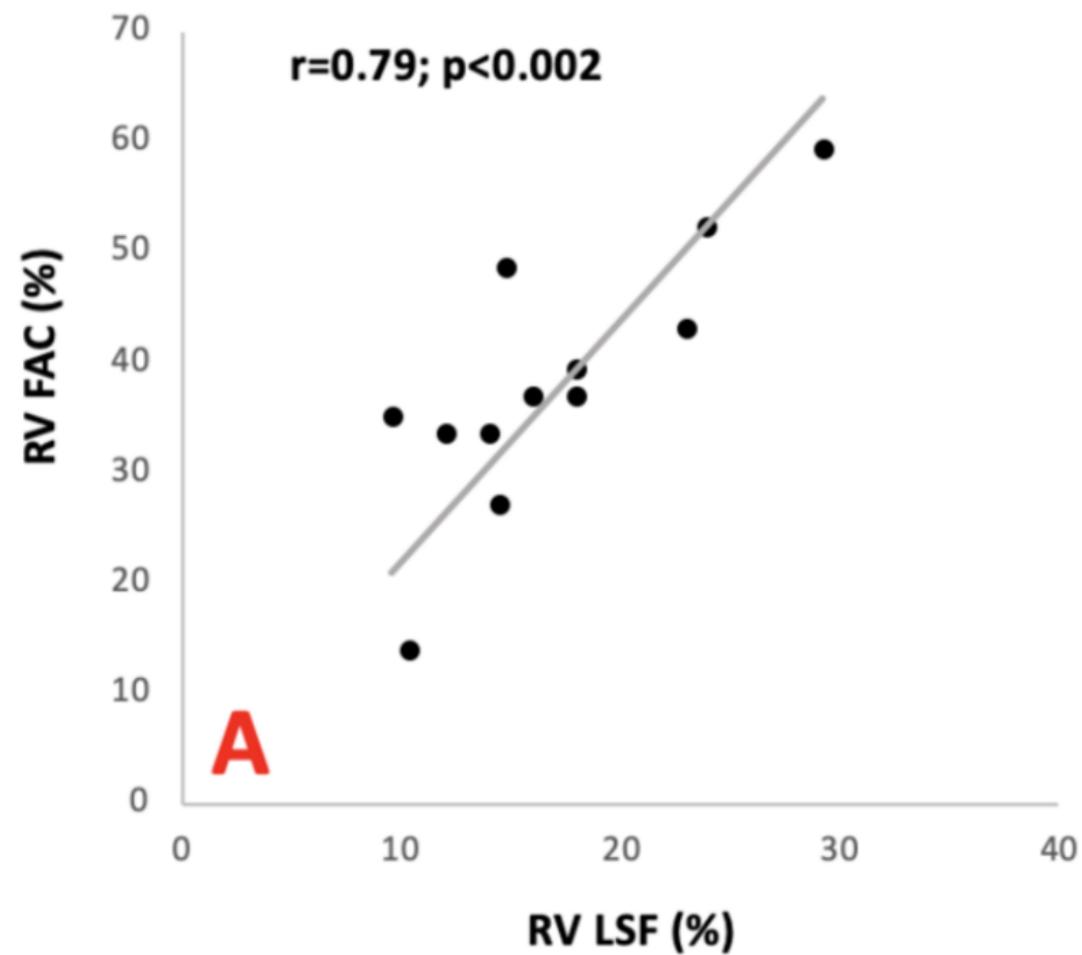
54 patients under mechanical ventilation

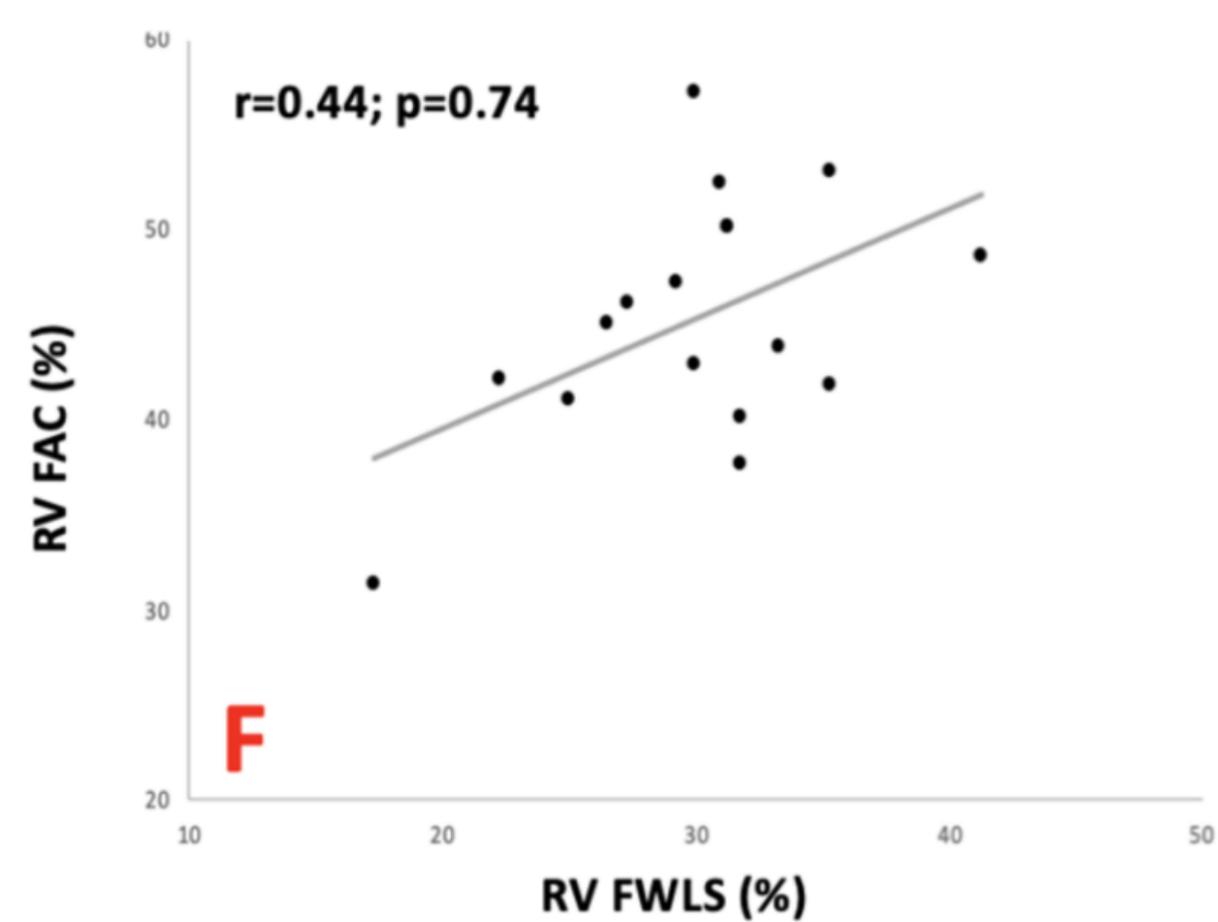
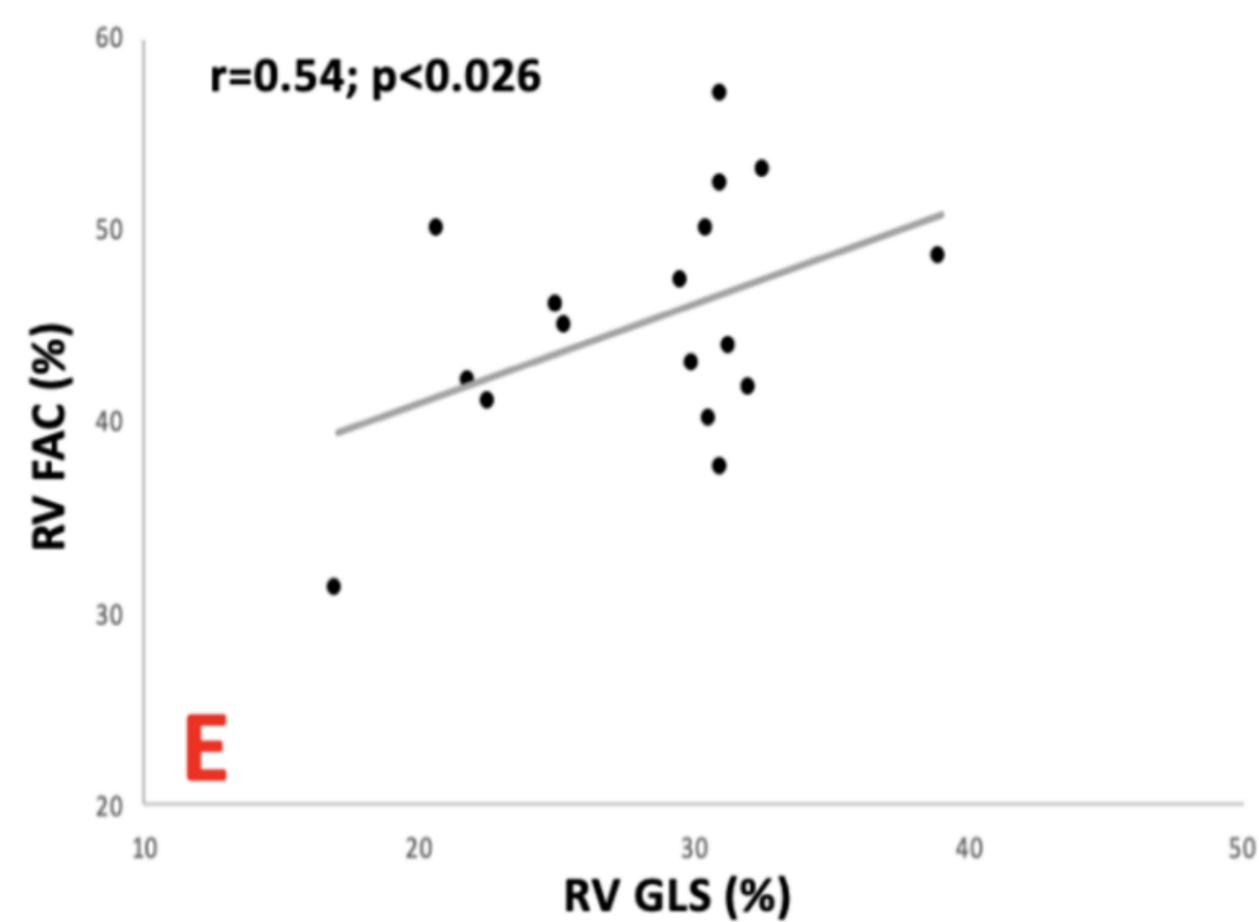
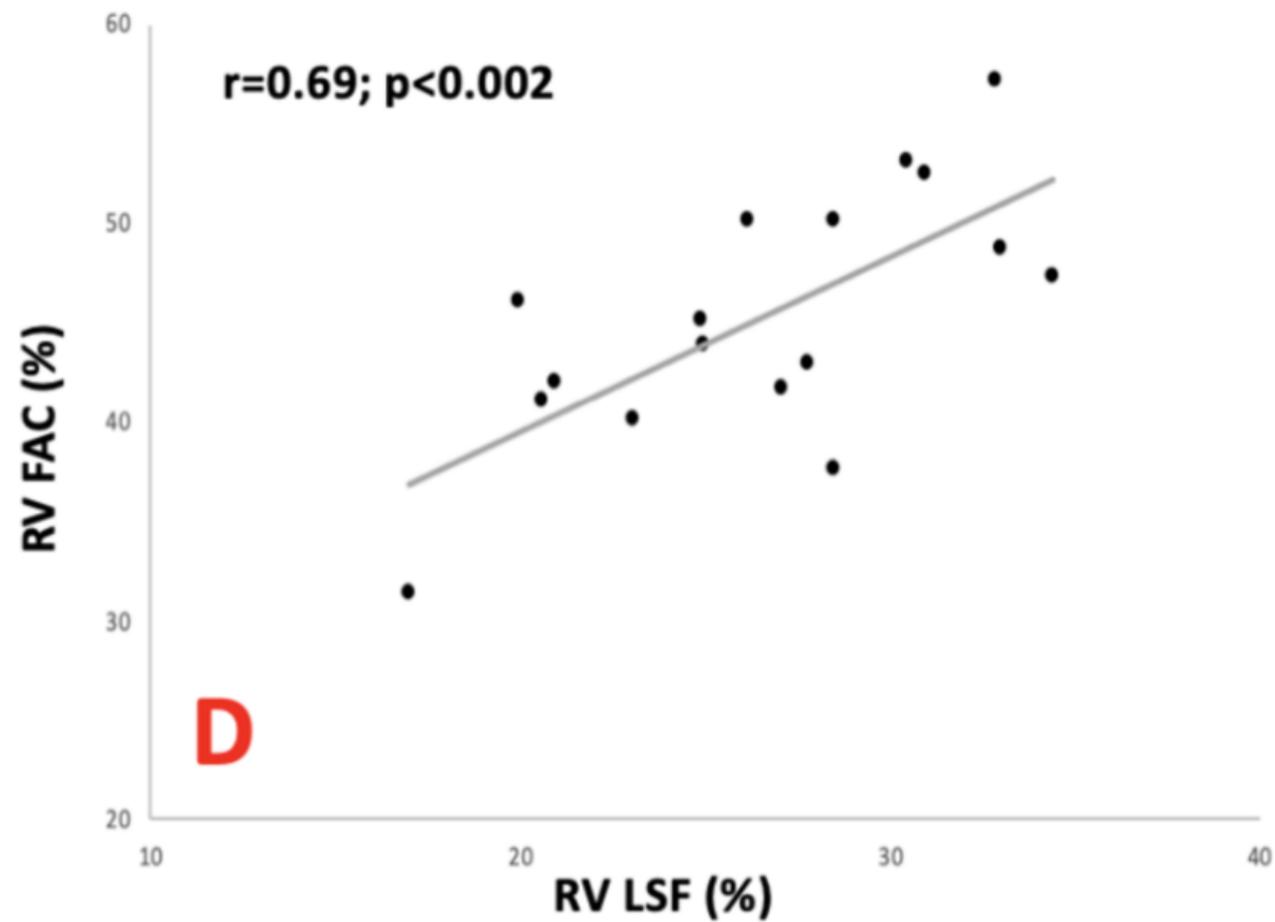
2 mild ARDS related to COVID-19 infection  
5 emergency surgery no related to COVID-19 pneumomia

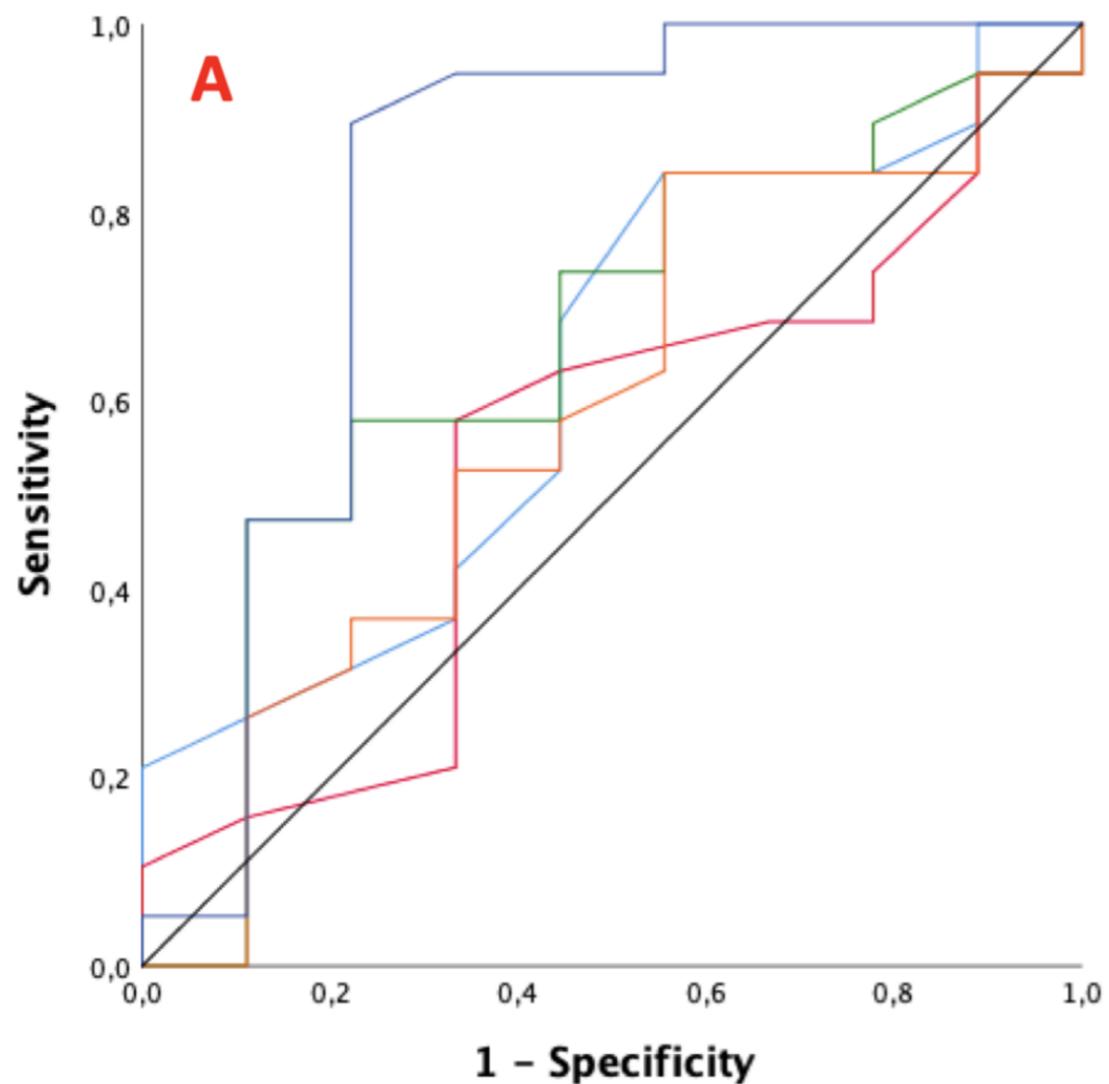
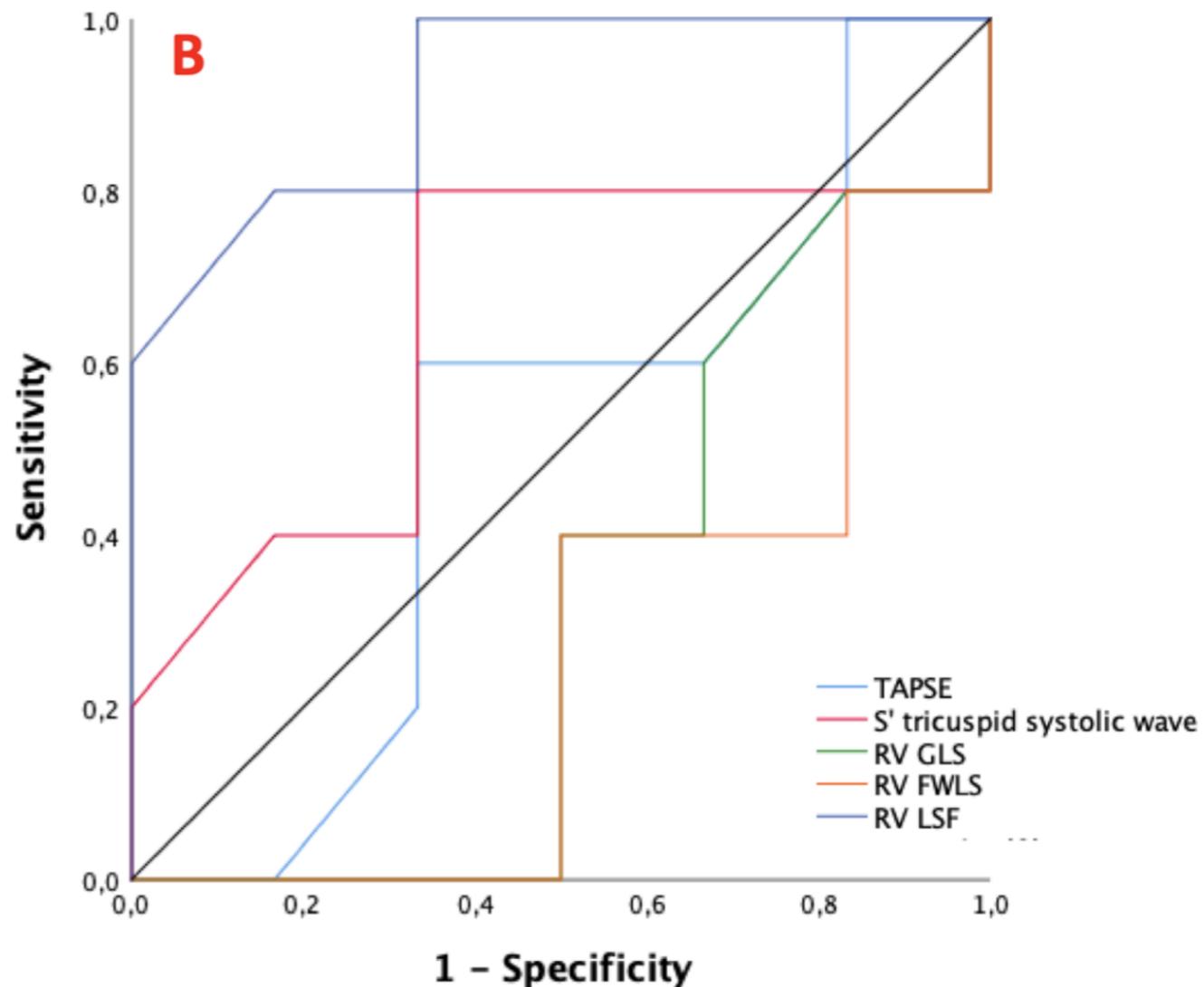
47 patients with moderate to severe ARDS under mechanical ventilation

14 ECMO  
1 patient with permanent ventricular pacing  
2 patients with previous right ventricular dysfunction  
1 patient with contraindication to TEE

29 patients





**Overall Population****ACP group**

**Table 1 Demographic and echocardiographic data.**

<b>Variables</b>	<b>No ACP (n=17)</b>	<b>ACP (n=12)</b>	<b>p</b>
Age (years)	64 [61-70]	62 [57-64]	0.18
BMI (kg.m <sup>-2</sup> )	30.5 [27-33]	30 [28-34]	0.98
Male gender (n; %)	12 (70)	10 (83)	0.65
SOFA score	8 [5.5-11.5]	7 [4.5-8.5]	0.25
<b>Ventilator settings during TTE/TEE</b>			
Tidal volume (ml.kg <sup>-1</sup> )	6.0 [5.7-6.2]	6.2 [6.0-7.0]	0.11
PaO <sub>2</sub> /FiO <sub>2</sub> (mmHg)	133 [84-191]	133 [106-161]	0.90
Positive end expiratory pressure, (cmH <sub>2</sub> O)	13 [12-15]	12 [12-16]	0.68
Plateau pressure (cmH <sub>2</sub> O)	26 [25-29]	27 [24-29]	0.62
Respiratory system Compliance (ml.cmH <sub>2</sub> O <sup>-1</sup> )	30.3 [28.1-36.2]	33.8 [29.3-38.3]	0.68
<b>Pulmonary embolism, (n; %)</b>	1 (6)	1 (8)	-
<b>Biological data before TTE/TEE</b>			
Lactate (mmol <sup>-1</sup> )	1.7 [1.2-2.3]	1.6 [1.4-1.9]	0.83
BNP (pg.ml <sup>-1</sup> )	55 [28-99]	64 [43-183]	0.34
Troponine Tc HS (ng.ml <sup>-1</sup> )	16 [7-44]	50 [32-229]	<b>0.03</b>
Procalcitonin (µg.l <sup>-1</sup> )	0.4 [0.2-1.4]	1.8 [0.5-4.0]	<b>0.04</b>
<b>RV Parameters</b>			
RV basal dimension (mm)	46 [35-51]	53 [50-53]	<b>0.02</b>
RV mid-cavity dimension (mm)	35 [30-43]	41 [40-42]	<b>0.03</b>
RV longitudinal dimension (mm)	69 [55-78]	79 [78-80]	0.18
RV EDA (cm <sup>2</sup> )	16 [14-19]	22 [19-24]	<b>0.002</b>
RV EDA indexed to BSA (cm <sup>2</sup> .m <sup>-2</sup> )	7.0 [6.0-9.4]	9.1 [8.8-10.4]	<b>0.01</b>
RV ESA (cm <sup>2</sup> )	8 [7-11]	12.5 [11-16]	<b>&lt;0.0001</b>
RV ESA indexed to BSA (cm <sup>2</sup> .m <sup>-2</sup> )	3.4 [2.8-4.4]	5.6 [4.8-6.9]	<b>&lt;0.0001</b>
RV EDA/LV EDA	0.51 [0.48-0.55]	0.77 [0.69-0.83]	<b>&lt;0.0001</b>
Septal dyskinesia, (n; %)	0 (0)	12 (100)	<b>&lt;0.0001</b>
RA volume (ml)	41 [31-48]	40 [30-60]	0.60
RA volume indexed to BSA (ml.m <sup>-2</sup> )	19 [15-22]	19 [16-29]	0.85
RV stroke volume indexed to BSA (ml.m <sup>-2</sup> )	33 [27-35]	32 [27-40]	0.94
AT <sub>RVOT</sub> (msec)	90 [80-120]	95 [82-145]	0.72
RA pressure (mmHg)			
- > 15 mmHg	4 (23)	3 (25)	0.58
- < 15 mmHg	13 (76)	8 (66)	-
Left ventricular ejection fraction (%)	62 [53-74]	66 [58-71]	0.36
<b>Classical RV Systolic Function Parameters</b>			
TAPSE (mm)	24 [17-25]	21 [19-25]	0.07
RV- S' (cm.s <sup>-1</sup> )	16 [13-19]	18 [14-21]	0.49

RV-FAC (%)	45 [42-52]	37 [33-48]	0.07
RV dysfunction (RV-FAC <35%), (n; %)	3 (18)	7 (58)	0.03
<b>2D-STE parameters</b>			
RVGLS (%)	-30.3 [24.6-31.6]	-18.5 [16.2-18.5]	<b>&lt;0.001</b>
RVFWLS (%)	-31.0 [25.5-32.5]	-19.4 [16.6-24.0]	<b>&lt;0.001</b>
<b>TAD parameters</b>			
❖ TAD <sub>lat</sub> (mm)	21.7 [19.1-24.4]	14.6 [10.0-20.2]	<b>0.002</b>
❖ TAD <sub>sep</sub> (mm)	11 [9-14]	6.7 [5-8.2]	<b>&lt;0.001</b>
❖ RV-LSF (%)	27 [25-30]	17 [14-22]	<b>&lt;0.001</b>

Continuous variables are expressed as median [interquartile range] and categorical variables as number (percentage). **Comparison was made between ACP and non-ACP group. P<0.05 was considered as significant**

**2D-STE:** bi-dimensionnel speckle tracking echocardiography. **ACP:** acute cor pulmonale. **AT<sub>rvot</sub>:** right ventricular outflow tract acceleration time. **BMI:** body mass index. **BNP:** brain natriuretic peptide. **EDA:** end diastolic area. **ESA:** end systolic area. **FAC:** fractional area change. **LV:** left ventricle. **RA:** right atrium. **RV:** right ventricle. **RVFWLS:** right ventricle free wall longitudinal strain. **RVGLS:** RV global longitudinal strain. **RV LSF:** RV longitudinal shortening fraction. **TAPSE:** tricuspid annular plane systolic excursion. **TEE:** transoesophageal echocardiography. **TAD:** Tricuspid annular displacement **TTE:** transthoracic echocardiograph

Table 2. Reproducibility of 2D-STE parameters

2D-STE parameters	ICC for intra-operator	IC95%	ICC for inter-operator	IC95%
<i>TAD parameters</i>				
<b>RV-LSF (%)</b>	<b>0.96</b>	<b>0.74-0.98</b>	<b>0.93</b>	<b>0.74-0.98</b>
<b>TAD<sub>lat</sub> (mm)</b>	<b>0.98</b>	<b>0.93-0.99</b>	<b>0.89</b>	<b>0.58-0.97</b>
<b>TAD<sub>sep</sub> (mm)</b>	<b>0.96</b>	<b>0.85-0.98</b>	<b>0.93</b>	<b>0.73-0.98</b>
<i>Strain parameters</i>				
<b>RVGLS (%)</b>	<b>0.92</b>	<b>0.72-0.98</b>	<b>0.92</b>	<b>0.68-0.98</b>
<b>RVFWLS (%)</b>	<b>0.88</b>	<b>0.6-0.97</b>	<b>0.84</b>	<b>0.37-0.96</b>

**2D-STE:** bi-dimensionnel speckle tracking echocardiography; **RVFWLS:** Right ventricle free wall longitudinal strain; **RVGLS:** Right ventricle global longitudinal strain. **RV-LSF:** Right ventricle longitudinal shortening fraction. **TAD:** Tricuspid annular displacement.

