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FEATURES OF ECHOCARDIOGRAPHIC STUDY IN PATIENTS WITH COVID-19

Novel coronavirus infection has become one of urgent health problems of the 21st century. The associated disorders often result in the development of cardiopulmonary pathology, which requires creation of a new paradigm in diagnosis and treatment. Studies performed during the pandemic have demonstrated an important role of echocardiography (EchoCG) in diagnosis of right ventricular (RV) dysfunction in patients with respiratory insufficiency in COVID-19. The analysis of EchoCG parameters with a high prognostic value showed that in EchoCG, a special attention should be paid to right heart dimensions, RV contractility, and pulmonary artery (PA) systolic pressure, which are the most sensitive indexes of RV afterload and indirect markers of pulmonary disease severity. RV FAC can be recommended for evaluation of the RV systolic function as the most informative variable. Also, it was demonstrated that the RV longitudinal strain has an additional significance for early identification of signs of systolic dysfunction and risk stratification in patients with COVID-19. In addition to the effectiveness and reproducibility of this method, an important advantage of EchoCG is its availability, possibility of saving images for remote interpretation by other specialists, and tracking changes in morphological and functional parameters of the heart. Thus, the analysis of international literature suggests that EchoCG plays an important role in prediction of severe cardiopulmonary disorders and timely selection of the treatment for patients with COVID-19. For these reasons, EchoCG should serve as an additional method of clinical evaluation, particularly in persons with moderate or severe disease.

Keywords Echocardiography; right ventricular dysfunction; COVID-19; predictor of adverse outcome; right ventricular longitudinal strain

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Introduction

The novel coronavirus infection has become one of the most pressing health issues of the 21st century. The pandemic of CORonaVirus Disease 2019 (COVID-19) not only caused significant changes in the nature of socio-economic relations in society but set specific tasks for medicine to develop of new science-based approaches for the diagnosis and effective treatment of COVID-19. The complexity of COVID-19 treatment is due to the fact that the developing disorders often cause pulmonary and cardiac comorbidities, which requires creating a new paradigm in the diagnosis and treatment of cardiopulmonary disorders. In this regard, predictive diagnosis to predict the risk of life-threatening complications and adverse outcomes of the disease is becoming of great importance.

Cardiovascular complications

SARS-CoV-2 causes not only lung damage, but also causes direct or indirect life-threatening structural and functional damage to the cardiovascular system [1, 2]. The direct effect of the virus on the myocardium, and the toxic effect of cytokines released during infection with simultaneous development of myocarditis, acute

myocardial infarction, or stress cardiomyopathy, may be the primary link in the formation of cardiovascular disorder in COVID-19 [3, 4].

Moreover, cardiac disorders may be associated with acute lung damage causing secondary right ventricular (RV) dysfunction [3]. This may result from acute respiratory distress syndrome (ARDS) being the most severe stage of acute lung damage, acute pulmonary embolism associated with blood clotting disorders, venous thromboembolism. The development of acute lung injury syndrome in COVID-19 significantly worsens the prognosis. According to the meta-analysis [5], mortality in ARDS of different origin is about 45%, by in ARDS associated with COVID-19, it is particularly high and can reach 85% [6–8]. The high incidence and severity of cardiovascular complications in COVID-19 is most likely to explain this discrepancy.

Clinical trials confirm that patients with cardiovascular disorders (coronary artery disease, hypertensive heart disease, diabetes mellitus, valvular or congenital heart diseases) face the highest risk of developing complications [9]. Serious cardiac complications are likely to aggravate patient's condition due to a reduced cardiovascular functional

reserve [3]. Moreover, hypermetabolism leads in systemic inflammation syndrome to increased oxygen consumption, aggravates myocardial ischemia and heart failure. This suggests that infectious stress in COVID-19 can quickly shove a patient with heart failure or coronary artery disease to the decompensated state [8].

Echocardiography in the COVID-19 era

Echocardiography has been focused on the functional evaluation of the left heart for several decades. Many researchers noted the long-term absence of changes in the left heart in most patients with COVID-19 [10–13], which contributed to an underestimation of the significance of echocardiography at the dawn of the SARS-CoV-2 spread. Additionally, ignorance and underestimation of the pathophysiological and clinical value of structural and functional RV changes also limited the use of echocardiography in COVID-19 patients. The above reasons, as well as the prevention of coronavirus transmission and the desire to protect medical personnel, have led to limited use of echocardiography. But, given the high frequency of cardiovascular complications, it became increasingly difficult to follow initial guidelines [14, 15].

The use of transesophageal echocardiography in COVID-19 patients was unreasonably limited, since the exhaled dispersion of the air mixture aerosols during the procedure increases the risk of infection among the staff [3, 16]. At the same time, the frequent lack of adequate transthoracic imaging in patients with ARDS and/or mechanical ventilation does not allow completely abandoning the use of transesophageal access [17].

The initial provisions with respect to transthoracic echocardiography have changed. New research studies carried out by 2021 (COVID-19 third wave) made it possible to supplement the echocardiography protocol with conceptual diagnostic concepts of the examination technique, the significance of parameters, and the assessment of the risk of life-threatening disorders. It is now recognized that transthoracic echocardiography represents a balance of benefit and risk, especially for patient routing in ER, when determining treatment strategy, and when left and/or right ventricular dysfunction is suspected [14]. Particular attention is paid to the benefits of focus assessed transthoracic echocardiography in critical COVID-19 patients with unstable hemodynamics, when echocardiography is becoming more important for clinical decision-making [16, 18, 19].

The understanding of the diagnostic algorithm has also changed significantly during the pandemic. Ac-

cording to data accumulated over the past decades, a decrease in the RV performance is an independent predictor of complicated disease and mortality in patients with heart failure, pulmonary hypertension, coronary artery disease, left ventricular (LV) dysfunction, congenital or acquired heart valve diseases [20–22]. Studies conducted during the COVID-19 pandemic have expanded the understanding of the real possibilities of predicting adverse outcomes in patients with COVID-19 and right ventricular dysfunction [10, 23].

Echocardiography protocol in patients with COVID-19

The use of the standard protocol of common echocardiographic parameters has limited information content [23] due to the complex irregular form of the RV and rapidly changing hemodynamics during the progression of COVID-19 [21]. There is still no standardized protocol for echocardiography approved by the scientific communities to assess the cardiopulmonary system in COVID-19 patients. Nevertheless, given the available information, we sought to identify the most informative echocardiographic parameters worth of attention in patients with COVID-19.

Of course, the traditional echocardiographic parameters are mainly used: LV ejection fraction and volumetric and linear parameters of the heart chambers. But, since the RV better reflects the state of the pulmonary system in COVID-19 patients and the relationship of hospital mortality with the RV dilation has been shown [14], the echocardiography protocol should include an assessment of dimensions especially of the right chambers [24, 25]. It is also necessary to assess the RV systolic function using such indicators as fractional area change (FAC), RV myocardial velocity (S'), tricuspid annular plane systolic excursion (TAPSE); RV myocardial performance index, or the Tei index, as well as possibly indicators the RV myocardial strain (right ventricular free wall longitudinal strain (RVFWLS), and RV global longitudinal strain (GLS). Assessment of pulmonary hemodynamics and the measurement of pulmonary artery (PA) pressure should be mandatory (Table 1).

Morphometric analysis of the right heart

Morphometric analysis is the primary way to assess the right heart, including in patients with acute lung tissue damage. The reservoir function of the right chambers compensates for the increased afterload, which is expressed in compensatory dilation of both

Table 1. Echocardiographic assessment of the right heart

Dimensions of the right heart chambers
RA linear and volumetric indicators
RV linear dimensions
RV area
RV/LV area ratio
RV systolic function
RV fractional area change (RVFAC)
Tricuspid annular systolic velocity (S')
Tricuspid annular plane systolic excursion (TAPSE)
RV myocardial performance index (Tei index)
Myocardial strain indicators (RVFWLS, RVGLS)
Parameters of pulmonary hemodynamics
PA systolic pressure
Mean PA systolic pressure
Pulmonary vascular resistance

RA, right atrium; RV, right ventricle, LV, left ventricle, RVFAC, right ventricular fractional area change; TAPSE, tricuspid annular plane systolic excursion; RVFWLS, right ventricular free wall longitudinal strain; RVGLS, right ventricular global longitudinal strain; PA, pulmonary artery.

the right ventricle and right atrium. As the pulmonary resistance increases, the RV dilates, the absolute values of the RV dimensions and the ratio of the RV area to the LV area increase, which can approach 1,0 and even surpass it (normal is 0.6) (Figure 1). And in this case, the RV can form the apex of the heart.

According to Argulian et al. [26], RV dilation was often detected by focus assessed transthoracic echocardiography in hospitalized patients with COVID-19. According to the univariate analysis, COVID-19

mortality was associated with mechanical ventilation, cardiotoxic support, RV dilation, and in the multivariate analysis, RV dilation was the only variable associated with an unfavorable outcome (odds ratio (OR) 4.5; 95% confidence interval (CI): 1.5–13.7; $p=0.005$).

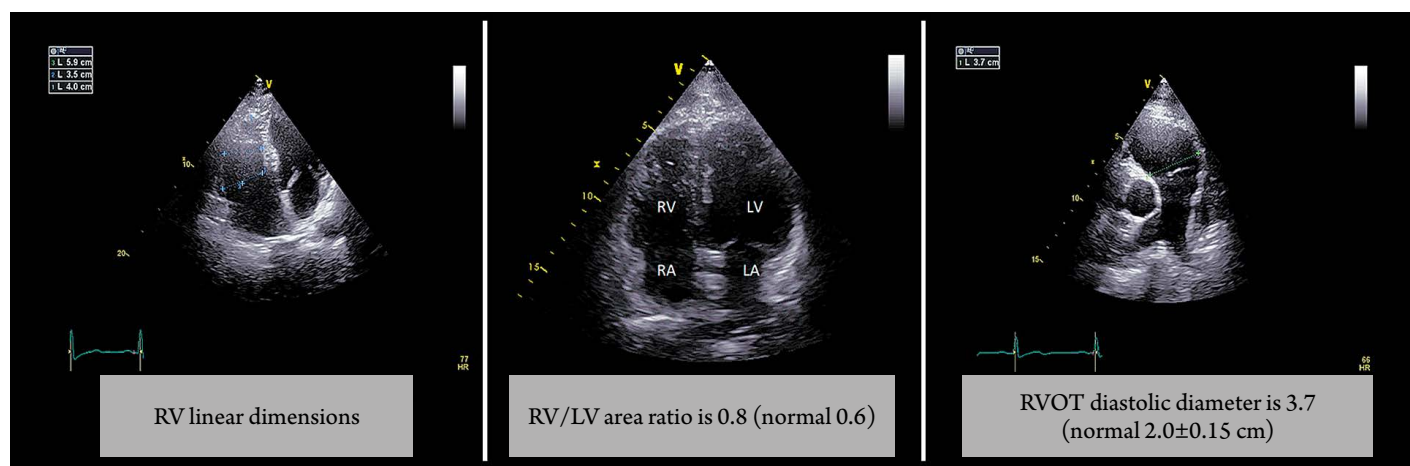
Parameters of the RV systolic function

TAPSE is the most common and easily reproducible method of assessing the RV systolic function [27]. Decreased excursion (<17 mm) is indicative of the RV systolic dysfunction [28].

According to a systematic review and meta-analysis (Martha et al., 2021) that included 641 patients with COVID-19, a 1 mm decrease in TAPSE was associated with higher mortality (hazard ratio (HR) 1.24; 95% CI: 1.18–1.31; $p<0.001$; in the combined adjusted model HR 1.21; 95% CI: 1.11–1.33; $p=0.001$) [29]. The mean TAPSE difference between the living and deceased patient groups was 3.74 mm, but it is worth noting that in only two of seven studies, this indicator was lower than the reference. In the rest of the papers, TAPSE varied from 18 to 21 mm in the group of unfavorable outcomes.

According to the Chinese researchers, TAPSE decreased in only 4% of hospitalized patients with COVID-19 [30]. It is noteworthy that, reduced TAPSE was observed in some studies mainly in terminal COVID-19 patients, among whom the values often surpassed the threshold, which is likely to be due to several drawbacks of this parameter, including most particularly the assessment of the RV longitudinal function only at the basal level (see supplementary materials on the journal's website). Severe tricuspid regurgitation (TR) can also lead to overestimation of TAPSE [2].

Figure 1. Morphometric analysis of the right ventricular dimensions



RV, right ventricle; LV, left ventricle; RVOT, right ventricular outflow tract.

Tissue Doppler allows measuring the tricuspid annular systolic velocity (S'). Normally, this indicator should exceed 9.5 cm/s in pulse-wave tissue Doppler [28]. Pressure overload is accompanied in ARDS by the appearance of TR and is likely to result in an overestimation of S' [2]. Moreover, the use of this indicator in patients with rapid pressure overload is limited, like in the case of TAPSE, to the assessment of basal RV segments [31] and longitudinal RV function.

Several studies demonstrated that the RV fractional area change (FAC) is well correlated with right ventricular ejection fraction (RVEF) as shown by MRI [32, 33]. This value normally exceeds 35% [28].

In the study by Barman et al., this indicator exceeded the threshold value despite a statistically significant decrease in RVFAC in the severe COVID-19 group (41% versus 45% in the living patient group) and the signs of left ventricular dysfunction [34]. Similar data were obtained by Golukhova et al. who determined echocardiographic predictors of adverse outcome in COVID-19 patients [23], according to which there was a statistically significant decrease in RVFAC among deceased patients (45.4% versus 52.7% in the living patient group). Nevertheless, the values often turned out to be above normal, i.e., 35%, in the group of COVID-19 patients with severe course or adverse outcome.

Bleakley et al. on the contrary showed a significantly higher percentage of patients with RV dysfunction identified by RVFAC [35]. However, they studied the right ventricular dysfunction phenotype in critical patients with ARDS of coronaviral origin, in which 42.2% of whom veno-venous extracorporeal membrane oxygenation was used. The authors suggested that a radial disorder (from the periphery to the center of the cavity) rather than a longitudinal one (from the heart base to its apex) is the dominant RV dysfunction phenotype in such patients. Which is why such parameters of the longitudinal function assessment as TAPSE and RV systolic myocardial velocity of (S') do not carry adequate information due to hyperdynamics, possibly in response to radial dysfunction. RVFAC in combination with PA systolic pressure (RV interface with a pulmonary circulation) is more preferable.

RV myocardial performance index (Tei index) could be a more accurate parameter for assessing RV systolic function. Normally, RV Tei index does not exceed 0.40 in pulse-wave Doppler and 0.55 in pulse-wave tissue Doppler [27]. However, increased PA pressure leads to pseudonormalization of this indicator, which is a significant drawback of this parameter for patients with increasing pulmonary resistance [36].

It should be noted that RV ejection fraction depends largely on load conditions, and therefore cannot be used as a reliable criterion for assessing the RV wall motion in patients with severe dilation or during pressure overload, which is common among patients with COVID-19. New echocardiographic techniques, including 2D STE and 3D echocardiography, allowed achieving high accuracy of RV functional evaluation comparable to MRI, which is the gold standard for RV imaging and evaluation [37]. However, 3D analysis of RV requires special software and directly depends on the image quality. Moreover, the dependence on the load is a significant drawback of RV 3D modeling, which can lead in severe dilation to the incomplete inclusion of the whole RV in the pyramidal form data set, and ultimately result in poor accuracy of 3D calculations. Thus, the inclusion of a three-dimensional analysis in the focus assessed protocol for COVID-19 patients is unreasonable in the absence of information about the prognostic value [28] and the existing limitations of the method.

The visualization of myocardial strain is a modern and promising technique for assessing the RV function and the mechanics of the RV myocardium [10, 38, 39]. Myocardial strain is a change in the object relative to its initial form [28]. Echocardiographic evaluation of RV strain can be performed using tissue Doppler imaging (TDI) or two-dimensional speckle tracking echocardiography (2D STE). Both methods are considered reproducible and relatively accurate to differentiate between different physiological and pathological conditions [40]. STE allows analyzing speckle track during myocardial shortening. Speckles are grains, but, in fact, they form a unique ultrasonic picture, which remains relatively stable throughout the cardiac cycle and thus recognizable for the software. Each RV segment can be analyzed separately. Mean RVFW or RV (including septal segments) strain can also be calculated. Thus, this technique allows measuring the performance of each segment separately. Unlike Doppler imaging, STE speckle tracking does not depend on the scanning angle, and the myocardial strain can be tracked in any direction [28].

It has been convincingly proved in several studies that the analysis of the RV longitudinal strain is a powerful tool for predicting the unfavorable course of various diseases [10, 23, 41, 42]. An important advantage of assessing the longitudinal deformation of the free wall of the RV (RVFWLS) is the independence of its predictive value from the LV global systolic function [10] and a higher predictive value compared to the right ventricular global longitudinal strain

(RVGLS) in patients with COVID-19 [43]. Moreover, the non-Doppler imaging technique was shown to be superior in monitoring of the RV performance [2] and can be applied in clinical algorithms aimed at preventing progressive RV dysfunction in COVID-19 patients [23].

LV dysfunction may be secondary to RV pressure and/or volume overload due to ventricular interdependence [44]. Of interest is a study, in which a comparative analysis of biventricular myocardial strain (LVGLS, RVFWLS, RVGLS) was conducted in patients with compensated and unfavorable course of COVID-19 [45]. All patients had reduced LVGLS, while RVFWLS and RVGLS were significantly decreased only in patients with adverse outcomes. Mean RVGLS and RVFWLS were $10.2 \pm 3.7\%$ and $9.8 \pm 3.8\%$, respectively, in the adverse outcome group, $20.3 \pm 6.1\%$ ($p=0.007$) and $21.5 \pm 6.5\%$ ($p=0.007$), respectively, in the group of patients with the compensated course of the disease.

The meta-analysis by Wibowo et al. (2021) showed that lower LVGLS and RVFWLS were independently correlated with adverse outcome in COVID-19 and a 1% decrease in LVGLS and RVFWLS was associated with a 1.3-fold and 1.24-fold increase in mortality, respectively [42].

Baycan et al. determined the following predictors of adverse outcome in patients with COVID-19: LVGLS $> -15.2\%$ (OR=8.34, area under the curve (AUC)=0.83, sensitivity=77%, specificity=75%), RVFWLS $> -18.45\%$ (OR=6.23, AUC=0.77, sensitivity=72%, specificity=66%) [43].

A large cohort study conducted during the COVID-19 pandemic showed a high prognostic value of RVFWLS in the assessment of an unfavorable prognosis, superior to TAPSE or RV systolic myocardial velocity (S') [10]. The authors detected signs of RV dilation and RV systolic dysfunction in deceased patients and identified RVFWLS $< 23\%$ (in absolute values) as an independent predictor of hospital mortality according to multivariate analysis (AUC=0.87; sensitivity=94.4%, specificity=64.7%, $p<0.001$).

Lassen et al. [46] observed a decrease in systolic function of both ventricles in hospitalized patients with COVID-19. Cox multivariate regression showed correlations between decreased TAPSE (HR 1.18; 95% CI: 1.07–1.31; $p=0.002$, a 1 mm decrease), LVGLS (HR 1.20; 95% CI: 1.07–1.35; $p=0.002$, a 1% decrease), and RVFWLS (HR=1.64; 95% CI: 1.02–2.66; $p=0.043$, a 1% decrease) and COVID-19 mortality.

The predictive capability of RV and LV longitudinal strain was confirmed in the study by the World Alliance Societies of Echocardiography [39]. The study included data of 13 sites. The following indicators were singled out of echocardiographic predictors of mortality in patients with COVID-19: LVGLS 16.7% and RVFWLS 20.2%. Thus, these values can be important markers and even predictors of the clinical course of COVID-19.

Evaluation of pulmonary hemodynamics

The most likely mechanism of the development of a concomitant disorder in COVID-19 patients is related to lung disease that disrupts the balance in oxygen delivery and consumption, elevates resistance of pulmonary vessels, and leads to the rapid development of pulmonary hypertension, which ultimately results in acute RV overload and dysfunction [47]. There were correlations between high PA systolic pressure and the disease severity, the transfer of patients to intensive care units, and the development of ARDS [48].

Pulmonary artery systolic pressure (PASP) is calculated by the peak TR gradient using the modified Bernoulli formula with the addition of estimated central venous pressure [27, 49]. Another option for assessing pulmonary hemodynamics is measuring mean pulmonary artery pressure (mPAP) using the formula proposed by Masuyama [50]. However, echocardiography may be accompanied in patients with pulmonary damage by acoustical disturbance from B-lines in the parasternal short axis of the heart base.

The RA pressure can be measured directly by the central venous catheter, but it is assessed most often in clinical practice by the inferior vena cava diameter and its response to inhalation [27, 51]. The estimated RA pressure does not exceed 20 mm Hg. However, according to a review by leading experts, the RA pressure may exceed 30 mm Hg (direct catheterization) in some patients with severe lung diseases [41], which can lead to a significant underestimation of the PA pressure. According to other authors, the correlation Doppler imaging and catheterization of the right heart shows acceptable variability [52, 53]. Anyway, echocardiography allows abandoning direct catheterization of the right heart in patients with COVID-19 given the high risk of bleeding during anticoagulant therapy and in order to reduce unnecessary procedures to evaluate pulmonary hypertension in patients with COVID-19 [48].

It is also possible to measure the echocardiographic equivalent of pulmonary vascular resistance (PVR) using the ratio of the peak TR velocity (m/s) to the

integral of linear velocity with respect to time (VTI) in the RV outflow tract region [54].

Analysis of the coupling of RV with the pulmonary circulation allows regarding RV and PA as a single cardiopulmonary system [35, 55]. Modern echocardiographic technologies make it possible to determine changes in the coupling without a complex scheme for RV pressure-volume plotting using the RV systolic function with respect to the pulmonary pressure measured by echocardiography [35, 55, 56]: 1) TAPSE/PASP, 2) FAC/mPAP or PASP. These formulas were proposed as surrogates for the invasive indicators of the RV-PA coupling Ees/Ea (systolic elastance/arterial elastance) [56, 57]. Reduced coupling is indicative of lower capability of the RV to contract during the increasing hydraulic load [58, 59] and the development of maladjustment processes [55], and also correlates with the likelihood of unfavorable course of various pathological conditions [35, 55, 60]. According to Bleakley et al., the measurement of the RV-PA coupling provides additional information on the severity of RV functional disorders in ARDS associated with COVID-19 [35].

Limitations

The accumulated echocardiographic data of patients with COVID-19 have different weights and different evidence base due to the differences in examination techniques. Data heterogeneity is also considerably related to large differences in populations, ethnicity, the lack of reference test protocols, and the study of parameters in patients with COVID-19 of varying severity. Randomized trials with standardized protocols including comparative analyses with control groups are necessary to confirm the available data.

Conclusion

Echocardiography plays an important role in the prediction of severe cardiopulmonary disorders and making timely decisions on COVID-19 treatment strategy. Analysis of the RV dimensions, geometry, and function has become an important component of the evaluation of the condition of the heart and

contributes to clinical decision-making in patients with cardiorespiratory failure [16]. The increasing role of echocardiography is emphasized in the diagnosis of RV dysfunction in patients with refractory respiratory failure [34]. Transthoracic echocardiography is important for the clinical evaluation of patients with COVID-19, especially in moderate to severe disease, the monitoring of hospitalized patients with multiple lung tissue consolidation regions and ARDS [17]. Moreover, echocardiography showed that large volumes of mechanical ventilation and increased alveolar pressure could lead to the excessive RV afterload and elevated PASP [61], which contributed to changes in respiratory support and the application of protective ventilation in patients with COVID-19 [41].

Analysis of the findings of various studies of COVID-19 patients showed that the best-possible echocardiography protocol should be aimed at measuring the dimensions of the right heart, the RV contractile function, and pulmonary pressure, which are the most sensitive indicators of the RV afterload and indirect markers of the lung disease severity. Analysis of the RV strain contributes to the early identification of signs of systolic dysfunction and risk stratification in patients with COVID-19. However, as well as the effectiveness and reproducibility of the method, its availability, especially within most intensive care units, is the important aspect in the context of the ongoing pandemic. Thus, RVFAC can be recommended to assess the RV systolic function as the most informative indicator among the standard parameters of the RV functional state, especially in critical conditions.

It is important to note that the examinations should be performed by experienced specialists, which will reduce the duration of scanning and allow obtaining the best possible imaging quality. It is also reasonable to save images for remote interpretation by other specialists and monitoring changes in morphological and functional parameters of the heart [3].

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REFERENCES

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The Lancet*. 2020;395(10223):497–506. DOI: 10.1016/S0140-6736(20)30183-5
2. Golukhova E.Z., Slivneva I.V., Rybka M.M., Mamalyga M.L., Alekhin M.N., Klyuchnikov I.V. et al. Structural and functional changes of the right ventricle in COVID-19 according to echocardiography. *Creative Cardiology*. 2020;14(3):206–23. [Russian: Голухова Е.З., Сливнева И.В., Рыбка М.М., Мамалыга М.Л., Алехин М.Н., Ключников И.В. и др. Структурно-функциональные изменения правого желудочка при COVID-19 по данным эхокардиографии. *Креативная кардиология*. 2020;14(3):206–23]. DOI: 10.24022/1997-3187-2020-14-3-206-223
3. Capotosto L, Nguyen BL, Ciardi MR, Mastroianni C, Vitarelli A. Heart, COVID-19, and echocardiography. *Echocardiography*. 2020;37(9):1454–64. DOI: 10.1111/echo.14834

4. Picard MH, Weiner RB. Echocardiography in the Time of COVID-19. *Journal of the American Society of Echocardiography*. 2020;33(6):674–5. DOI: 10.1016/j.echo.2020.04.011
5. Máca J, Jor O, Holub M, Sklienka P, Burša F, Burda M et al. Past and Present ARDS Mortality Rates: A Systematic Review. *Respiratory Care*. 2017;62(1):113–22. DOI: 10.4187/respcare.04716
6. Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G et al. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy. *JAMA Internal Medicine*. 2020;180(10):1345–55. DOI: 10.1001/jamainternmed.2020.3539
7. Giustino G, Croft LB, Stefanini GG, Bragato R, Silbiger JJ, Vicenzi M et al. Characterization of Myocardial Injury in Patients With COVID-19. *Journal of the American College of Cardiology*. 2020;76(18):2043–55. DOI: 10.1016/j.jacc.2020.08.069
8. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *The Lancet*. 2020;395(10229):1054–62. DOI: 10.1016/S0140-6736(20)30566-3
9. Linschoten M, Peters S, Van Smeden M, Jewbali LS, Schaap J, Siebelink H-M et al. Cardiac complications in patients hospitalised with COVID-19. *European Heart Journal. Acute Cardiovascular Care*. 2020;9(8):817–23. DOI: 10.1177/2048872620974605
10. Li Y, Li H, Zhu S, Xie Y, Wang B, He L et al. Prognostic Value of Right Ventricular Longitudinal Strain in Patients With COVID-19. *JACC Cardiovascular Imaging*. 2020;13(11):2287–99. DOI: 10.1016/j.jcmg.2020.04.014
11. Bhatia HS, Bui QM, King K, DeMaria A, Daniels LB. Subclinical left ventricular dysfunction in COVID-19. *IJC Heart & Vasculture*. 2021;34:100770. DOI: 10.1016/j.ijcha.2021.100770
12. Hollenberg SM, Safi L, Parrillo JE, Fata M, Klinkhammer B, Gayed N et al. Hemodynamic Profiles of Shock in Patients With COVID-19. *The American Journal of Cardiology*. 2021;153:135–9. DOI: 10.1016/j.amjcard.2021.05.029
13. Alvarez-Garcia J, Lee S, Gupta A, Cagliostro M, Joshi AA, Rivas-Lasarte M et al. Prognostic Impact of Prior Heart Failure in Patients Hospitalized With COVID-19. *Journal of the American College of Cardiology*. 2020;76(20):2334–48. DOI: 10.1016/j.jacc.2020.09.549
14. Kirkpatrick JN, Mitchell C, Taub C, Kort S, Hung J, Swaminathan M. ASE Statement on Protection of Patients and Echocardiography Service Providers During the 2019 Novel Coronavirus Outbreak. *Journal of the American College of Cardiology*. 2020;75(24):3078–84. DOI: 10.1016/j.jacc.2020.04.002
15. Skulstad H, Cosyns B, Popescu BA, Galderisi M, Salvo GD, Donal E et al. COVID-19 pandemic and cardiac imaging: EACVI recommendations on precautions, indications, prioritization, and protection for patients and healthcare personnel. *European Heart Journal - Cardiovascular Imaging*. 2020;21(6):592–8. DOI: 10.1093/ehjci/jeaa072
16. Cameli M, Pastore MC, Soliman Aboumarie H, Mandoli GE, D'Ascenzi F, Cameli P et al. Usefulness of echocardiography to detect cardiac involvement in COVID-19 patients. *Echocardiography*. 2020;37(8):1278–86. DOI: 10.1111/echo.14779
17. Cresti A, Barchitta A, Barbieri A, Monte IP, Trocino G, Ciampi Q et al. Echocardiography and Multimodality Cardiac Imaging in COVID-19 Patients. *Journal of Cardiovascular Echography*. 2020;30(Suppl 2):S18–24. DOI: 10.4103/jcecho.jcecho_58_20
18. Zhang L, Wang B, Zhou J, Kirkpatrick J, Xie M, Johri AM. Bed-side Focused Cardiac Ultrasound in COVID-19 from the Wuhan Epicenter: The Role of Cardiac Point-of-Care Ultrasound, Limited Transthoracic Echocardiography, and Critical Care Echocardiography. *Journal of the American Society of Echocardiography*. 2020;33(6):676–82. DOI: 10.1016/j.echo.2020.04.004
19. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. *JAMA Cardiology*. 2020;5(7):802–10. DOI: 10.1001/jamacardio.2020.0950
20. Davlourous PA. The right ventricle in congenital heart disease. *Heart*. 2006;92(Suppl 1):i27–38. DOI: 10.1136/hrt.2005.077438
21. Haddad F, Doyle R, Murphy DJ, Hunt SA. Right Ventricular Function in Cardiovascular Disease, Part II: Pathophysiology, Clinical Importance, and Management of Right Ventricular Failure. *Circulation*. 2008;117(13):1717–31. DOI: 10.1161/CIRCULATIONAHA.107.653584
22. Murninkas D, Alba AC, Delgado D, McDonald M, Bilia F, Chan WS et al. Right ventricular function and prognosis in stable heart failure patients. *Journal of Cardiac Failure*. 2014;20(5):343–9. DOI: 10.1016/j.cardfail.2014.01.018
23. Golukhova E.Z., Slivneva I.V., Rybka M.M., Mamalyga M.L., Marapov D.I., Klyuchnikov I.V. et al. Right ventricular systolic dysfunction as a predictor of adverse outcome in patients with COVID-19. *Kardiologiya*. 2020;60(11):16–29. [Russian: Голухова Е.З., Сливнева И.В., Рыбка М.М., Мамалыга М.Л., Маратов Д.И., Ключников И.В. и др. Систолическая дисфункция правого желудочка как предиктор неблагоприятного исхода у пациентов с COVID-19. *Кардиология*. 2020;60(11):16–29]. DOI: 10.18087/cardio.2020.11.n1303
24. Hanley B, Jensen M, Osborn M. Emerging spectrum of COVID-19-related cardiopulmonary pathology in adults. *Diagnostic Histopathology*. 2021;27(8):317–24. DOI: 10.1016/j.jmpdh.2021.05.002
25. Buja LM, Zhao B, McDonald M, Ottaviani G, Wolf DA. Commentary on the spectrum of cardiopulmonary pathology in COVID-19. *Cardiovascular Pathology*. 2021;53:107339. DOI: 10.1016/j.carpath.2021.107339
26. Argulian E, Sud K, Vogel B, Bohra C, Garg VP, Talebi S et al. Right Ventricular Dilation in Hospitalized Patients With COVID-19 Infection. *JACC: Cardiovascular Imaging*. 2020;13(11):2459–61. DOI: 10.1016/j.jcmg.2020.05.010
27. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K et al. Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography. *Journal of the American Society of Echocardiography*. 2010;23(7):685–713. DOI: 10.1016/j.echo.2010.05.010
28. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L et al. Recommendations for Cardiac Chamber Quantification by Echocardiography in Adults: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *Journal of the American Society of Echocardiography*. 2015;28(1):1–39.e14. DOI: 10.1016/j.echo.2014.10.003
29. Martha JW, Pranata R, Wibowo A, Lim MA. Tricuspid annular plane systolic excursion (TAPSE) measured by echocardiography and mortality in COVID-19: A systematic review and meta-analysis. *International Journal of Infectious Diseases*. 2021;105:351–6. DOI: 10.1016/j.ijid.2021.02.029
30. Deng Q, Hu B, Zhang Y, Wang H, Zhou X, Hu W et al. Suspected myocardial injury in patients with COVID-19: Evidence from front-line clinical observation in Wuhan, China. *International Journal of Cardiology*. 2020;311:116–21. DOI: 10.1016/j.ijcard.2020.03.087
31. Jurcut R, Giusca S, La Gerche A, Vasile S, Ginhina C, Voigt J-U. The echocardiographic assessment of the right ventricle: what to do in 2010? *European Journal of Echocardiography*. 2010;11(2):81–96. DOI: 10.1093/ejehocardi/jep234
32. Agasthi P, Chao C, Siegel RJ, Pujari SH, Mookadam F, Venepally NR et al. Comparison of echocardiographic parameters with cardiac magnetic resonance imaging in the assessment of right ventricular function. *Echocardiography*. 2020;37(11):1792–802. DOI: 10.1111/echo.14877

33. Simsek E, Nalbantgil S, Ceylan N, Zoghi M, Kemal HS, Engin C et al. Assessment of right ventricular systolic function in heart transplant patients: Correlation between echocardiography and cardiac magnetic resonance imaging. Investigation of the accuracy and reliability of echocardiography. *Echocardiography*. 2017;34(10):1432–8. DOI: 10.1111/echo.13650
34. Barman HA, Atici A, Tekin EA, Baycan OF, Alici G, Meric BK et al. Echocardiographic features of patients with COVID-19 infection: a cross-sectional study. *The International Journal of Cardiovascular Imaging*. 2021;37(3):825–34. DOI: 10.1007/s10554-020-02051-9
35. Bleakley C, Singh S, Garfield B, Morosin M, Surkova E, Mandalia MS et al. Right ventricular dysfunction in critically ill COVID-19 ARDS. *International Journal of Cardiology*. 2021;327:251–8. DOI: 10.1016/j.ijcard.2020.11.043
36. Yoshifuku S, Otsuji Y, Takasaki K, Yuge K, Kisanuki A, Toyonaga K et al. Pseudonormalized doppler totalejection isovolume (Tei) index in patients with right ventricular acute myocardial infarction. *The American Journal of Cardiology*. 2003;91(5):527–31. DOI: 10.1016/S0002-9149(02)03299-X
37. Valsangiacomo Buechel ER, Mertens LL. Imaging the right heart: the use of integrated multimodality imaging. *European Heart Journal*. 2012;33(8):949–60. DOI: 10.1093/eurheartj/ehr490
38. Wright L, Dwyer N, Power J, Kritharides L, Celermajer D, Marwick TH. Right Ventricular Systolic Function Responses to Acute and Chronic Pulmonary Hypertension: Assessment with Myocardial Deformation. *Journal of the American Society of Echocardiography*. 2016;29(3):259–66. DOI: 10.1016/j.echo.2015.11.010
39. Karagodin I, Carvalho Singulane C, Woodward GM, Xie M, Tucay ES, Tude Rodrigues AC et al. Echocardiographic Correlates of In-Hospital Death in Patients with Acute COVID-19 Infection: The World Alliance Societies of Echocardiography (WASE-COVID) Study. *Journal of the American Society of Echocardiography*. 2021;34(8):819–30. DOI: 10.1016/j.echo.2021.05.010
40. Teske AJ, De Boeck BWL, Olimulder M, Prakken NH, Doevendans PAF, Cramer MJ. Echocardiographic Assessment of Regional Right Ventricular Function: A Head-to-head Comparison Between 2-Dimensional and Tissue Doppler-derived Strain Analysis. *Journal of the American Society of Echocardiography*. 2008;21(3):275–83. DOI: 10.1016/j.echo.2007.08.027
41. D'Alto M, Marra AM, Severino S, Salzano A, Romeo E, De Rosa R et al. Right ventricular-arterial uncoupling independently predicts survival in COVID-19 ARDS. *Critical Care*. 2020;24(1):670. DOI: 10.1186/s13054-020-03385-5
42. Wibowo A, Pranata R, Astuti A, Tiksnadi BB, Martanto E, Martha JW et al. Left and right ventricular longitudinal strains are associated with poor outcome in COVID-19: a systematic review and meta-analysis. *Journal of Intensive Care*. 2021;9(1):9. DOI: 10.1186/s40560-020-00519-3
43. Baycan OF, Barman HA, Atici A, Tatlisu A, Bolen F, Ergen P et al. Evaluation of biventricular function in patients with COVID-19 using speckle tracking echocardiography. *The International Journal of Cardiovascular Imaging*. 2021;37(1):135–44. DOI: 10.1007/s10554-020-01968-5
44. Alpert JS. The effect of Right Ventricular Dysfunction on Left Ventricular Form and Function. *Chest*. 2001;119(6):1632–3. DOI: 10.1378/chest.119.6.1632
45. Krishnamoorthy P, Croft LB, Ro R, Anastasius M, Zhao W, Gustino G et al. Biventricular strain by speckle tracking echocardiography in COVID-19: findings and possible prognostic implications. *Future Cardiology*. 2021;17(4):663–7. DOI: 10.2217/fca-2020-0100
46. Lassen MCH, Skaarup KG, Lind JN, Alhakak AS, Sengeløv M, Nielsen AB et al. Echocardiographic abnormalities and predictors of mortality in hospitalized COVID-19 patients: the ECHOVID-19 study. *ESC Heart Failure*. 2020;7(6):4189–97. DOI: 10.1002/ehf2.13044
47. Clerkin KJ, Fried JA, Raikhelkar J, Sayer G, Griffin JM, Masoumi A et al. COVID-19 and Cardiovascular Disease. *Circulation*. 2020;141(20):1648–55. DOI: 10.1161/CIRCULATIONAHA.120.046941
48. Golukhova E.Z., Slivneva I.V., Rybka M.M., Mamalyga M.L., Alekhin M.N., Klyuchnikov I.V. et al. Pulmonary hypertension as a risk assessment factor for unfavorable outcome in patients with COVID-19. *Russian Journal of Cardiology*. 2020;25(12):121–33. [Russian: Голухова Е.З., Сливнева И.В., Рыбка М.М., Мамалыга М.Л., Алехин М.Н., Ключников И.В. и др. Легочная гипертензия как фактор оценки риска неблагоприятного исхода у пациентов с COVID-19. *Российский кардиологический журнал*. 2020;25(12):121–33]. DOI: 10.15829/1560-4071-2020-4136
49. Hatle L, Angelsen BA, Tromsdal A. Non-invasive estimation of pulmonary artery systolic pressure with Doppler ultrasound. *Heart*. 1981;45(2):157–65. DOI: 10.1136/hrt.45.2.157
50. Masuyama T, Kodama K, Kitabatake A, Sato H, Nanto S, Inoue M. Continuous-wave Doppler echocardiographic detection of pulmonary regurgitation and its application to noninvasive estimation of pulmonary artery pressure. *Circulation*. 1986;74(3):484–92. DOI: 10.1161/01.CIR.74.3.484
51. Magnino C, Omedè P, Avenatti E, Presutti D, Iannaccone A, Chiarlo M et al. Inaccuracy of Right Atrial Pressure Estimates Through Inferior Vena Cava Indices. *The American Journal of Cardiology*. 2017;120(9):1667–73. DOI: 10.1016/j.amjcard.2017.07.069
52. Lanzarini L, Fontana A, Lucca E, Campana C, Klersy C. Non-invasive estimation of both systolic and diastolic pulmonary artery pressure from Doppler analysis of tricuspid regurgitant velocity spectrum in patients with chronic heart failure. *American Heart Journal*. 2002;144(6):1087–94. DOI: 10.1067/mhj.2002.126350
53. Lindqvist P, Soderberg S, Gonzalez MC, Tossavainen E, Heinein MY. Echocardiography based estimation of pulmonary vascular resistance in patients with pulmonary hypertension: a simultaneous Doppler echocardiography and cardiac catheterization study. *European Journal of Echocardiography*. 2011;12(12):961–6. DOI: 10.1093/ejehocardiography/er222
54. Opatowsky AR, Clair M, Afilalo J, Landzberg MJ, Waxman AB, Moko L et al. A Simple Echocardiographic Method to Estimate Pulmonary Vascular Resistance. *The American Journal of Cardiology*. 2013;112(6):873–82. DOI: 10.1016/j.amjcard.2013.05.016
55. Guazzi M, Dixon D, Labate V, Beussink-Nelson L, Bandera F, Cuttica MJ et al. RV Contractile Function and its Coupling to Pulmonary Circulation in Heart Failure With Preserved Ejection Fraction. *JACC: Cardiovascular Imaging*. 2017;10(10 Pt B):1211–21. DOI: 10.1016/j.jcmg.2016.12.024
56. Tello K, Wan J, Dalmer A, Vanderpool R, Ghofrani HA, Naeije R et al. Validation of the Tricuspid Annular Plane Systolic Excursion/Systolic Pulmonary Artery Pressure Ratio for the Assessment of Right Ventricular-Arterial Coupling in Severe Pulmonary Hypertension. *Circulation: Cardiovascular Imaging*. 2019;12(9):e009047. DOI: 10.1161/CIRCIMAGING.119.009047
57. Bashline MJ, Simon MA. Use of Tricuspid Annular Plane Systolic Excursion/Pulmonary Artery Systolic Pressure As a Non-Invasive Method to Assess Right Ventricular-PA Coupling in Patients With Pulmonary Hypertension. *Circulation: Cardiovascular Imaging*. 2019;12(9):e009648. DOI: 10.1161/CIRCIMAGING.119.009648
58. Kelly RP, Ting CT, Yang TM, Liu CP, Maughan WL, Chang MS et al. Effective arterial elastance as index of arterial vascular load in humans. *Circulation*. 1992;86(2):513–21. PMID: 1638719
59. Knai K, Skjaervold NK. A pig model of acute right ventricular afterload increase by hypoxic pulmonary vasoconstriction.

- BMC Research Notes. 2017;10(1):2. DOI: 10.1186/s13104-016-2333-7
60. Topilsky Y, Oh JK, Shah DK, Boilson BA, Schirger JA, Kushwa-ha SS et al. Echocardiographic Predictors of Adverse Outcomes After Continuous Left Ventricular Assist Device Implan-tation. JACC: Cardiovascular Imaging. 2011;4(3):211–22. DOI: 10.1016/j.jcmg.2010.10.012
61. Vieillard-Baron A, Price LC, Matthay MA. Acute cor pulmonale in ARDS. Intensive Care Medicine. 2013;39(10):1836–8. DOI: 10.1007/s00134-013-3045-2