CARDIOVASCULAR AND METABOLIC SCIENCE

Vol. 31 No. 4 October-December2020



Implementation of a new echocardiographic practice during the COVID-19 pandemic

Implementación de una nueva práctica ecocardiográfica durante la pandemia COVID-19

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Keywords:

Transthoracic echocardiography, transesophageal echocardiography, stress echocardiography, personal protective equipment, echocardiographic findings.

Palabras clave:

Ecocardiograma transtorácico, ecocardiograma transesofágico, ecocardiograma de estrés, equipo de protección personal, hallazgos ecocardiográficos.

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Received: 13/06/2020. Accepted: 27/11/2020.

ABSTRACT

Due to the COVID-19 (SARS-CoV-2) pandemic, healthcare logistics have changed abruptly and significantly in all medical specialties, of which cardiovascular services are no exception. Assessment of urgent and priority cases did not stop, both medical personnel and patients required adaptation of personal protective measures to prevent the spread of a highly contagious and potentially fatal virus for this vulnerable population with cardiovascular disease. In the time that has elapsed since the beginning of said pandemic to date, the health sector has become immersed in a fortuitous and challenging situation for its work environment. Considering that this virus could remain endemic, it is necessary to devise a protocol for a gradual and safe reincorporation of services at all levels of care. This document provides an update on recommendations for the return to a safe but no less efficient echocardiographic practice, based on expert opinions, some international guidelines along with evidence available until recently on several main echocardiographic findings in patients with cardiovascular disease by COVID-19, providing a general approach that can be adapted to the guidelines of each health institution in this country.

RESUMEN

REVIEW

Debido a la pandemia por el virus COVID-19 (SARS-CoV-2) la logística de atención hospitalaria ha cambiado de manera abrupta y significativa en todas las especialidades médicas, de entre las cuales, los servicios cardiovasculares no son la excepción. La valoración de casos urgentes y prioritarios no se detuvo, tanto el personal de salud como los pacientes requirieron adaptarse a las medidas de protección personal para evitar la diseminación de un virus altamente contagioso y potencialmente mortal para este grupo de población vulnerable con enfermedad cardiovascular. En el tiempo transcurrido desde el inicio de la pandemia hasta la actualidad, el sector salud se ha visto inmerso en una situación fortuita y desafiante para su ámbito laboral, considerando que el virus podría permanecer endémico, es necesario llevar a cabo un protocolo para la reincorporación de los servicios de todos los niveles de atención de manera paulatina v segura. Este documento proporciona una puesta al día en recomendaciones para el regreso a una práctica ecocardiográfica segura pero no menos eficiente, basada en opiniones de expertos, algunas guías internacionales y la evidencia disponible hasta fechas recientes sobre los principales hallazgos ecocardiográficos en pacientes con afección cardiovascular por COVID-19, proporcionando un enfoque general y que pueda adaptarse a las directrices de cada institución de salud en este país.

INTRODUCTION

The COVID-19 pandemic has revolutionized the entire world, generating a radical change in health care in general and a significant impact on the care of patients with cardiovascular disease, having to adapt abruptly with general protection measures and a total reorganization in its logistics to prevent the transmission of this virus while at the same time providing a continuum of care to cardiovascular emergencies at the beginning of the pandemic, considering that these are the leading cause of death worldwide.

How to cite: López-Rincón M, Guzmán-Ramírez D, Hernández-Hernández JM, Farías-Vergara S, Sahagún-Sánchez G. Implementation of a new echocardiographic practice during the COVID-19 pandemic. Cardiovasc Metab Sci. 2020; 31 (4): 145-155. https://dx.doi.org/10.35366/97548



Recent reports demonstrate a deleterious effect on the quality of care for all chronic diseases, including cardiovascular diseases, which at this time have been under-diagnosed due to the deferral of elective cardiovascular imaging studies for both screening and follow-up. Cardiovascular emergencies even record fatal outcomes associated with delays in transfers and even the population's fear of going to a hospital. This odyssey has been exhausting, ranging from having the ability to discern patients who should continue to receive care in person or at a distance according to their risk (based on clinical status and disease stage), to reinventing remote consultation care with complicated and costly systems that have had to be implemented in a short period of time to follow up on cardiovascular patients, methods for assortment of medication, among others, which is true telemedicine. Health professionals, amidst such chaos and work overload in the emergency departments, have had to set up respiratory triage units in practically every hospital in this country, with the purpose of classifying patients according to severity states of SARS-CoV-2 disease, and among these, early suspicion of cardiovascular affectation by COVID-19, as it can occur in up to 17-20% of cases.^{1,2}

Echocardiography, being a non-invasive imaging modality with high availability, and its ability to provide extensive and detailed information in real time, has become the first-line tool for cardiovascular diagnosis; however, due to the high contagiousness of the virus and its transmission mechanism, it has become a risky procedure due to the proximity with the patient for the performance of said examination.³⁻⁶ The requirements for imaging studies have decreased by 50-90% depending on the type of examination; among these transesophageal studies have been to be classified as high-risk because of their ability to generate aerosols that remain virtually suspended temporarily; stress studies with exercise have been deferred or replaced by other imaging modalities with less risk of exposure, by a possibility of contamination secondary to droplets or aerosols generated in the effort and cough.7-10

The echocardiographic departament has undergone adaptations, which includes the route of admission of every patient, the time for performance of studies, and an exhaustive and frequent cleaning of the equipment with chlorine solutions and other agents to minimize the spread of this virus.^{6,8,11} The echocardiograms should be done in the shortest time possible to minimize exposure, used a focused protocol limited to what is required and with echocardiographic views that provide more information, considering that in COVID-19 patients in mechanical ventilatory support in prone position only apical view can be adquired.^{2,12} This new pathology has also been incorporated to the echocardiographic etiologic range, learning in an accelerated way through this short period of time to identify severity factors and even some prognostic echocardiographic data in the follow-up of patients with COVID-19. Therefore, it will be a dynamic balancing process to provide essential cardiovascular care to the general population and the provision of care for the continuous fluctuations of patients who are suspected or positive for COVID-19.

The pandemic seems to be spreading with continuous incidence of cases in different regions of this country, it is imperative to achieve a balance between the risk of infection and the risk represented by any delay in diagnosis and management of cardiovascular diseases; This document provides strategies and considerations based on recommendations from the different international societies of echocardiography and cardiac imaging, as well as on the scientific evidence available so far on the usefulness of echocardiography in patients affected by SARS-CoV-2. With the objective of gradually reincorporating the usual functioning of echocardiography services in a phased manner, adopting all necessary measures and providing care to cardiovascular patients in a safe and efficient manner while the health emergency lasts.

General considerations

The re-establishment of the normal functioning of the departament should be carried out with close communication between the referring physicians, echocardiographic physicians and administrative staff acording to the following:

- Phase 2: selected studies in which its performance marks a change in the management or prognosis of each patient.
- Phase 1: most studies with maximum precautions, with a possibility of postponing stable patients in follow-up.
- Phase 0: all routine studies with pre-testing (if available) and personal protective equipment according to pandemic status.

Generally, it is recommended to schedule staggered appointments, in the case of multiple studies organize a single visit, apply a symptom guestionnaire in a telephone schedule appointments (Anexo 1). Upon arrival of each patient take body temperature and reapply symptom questionnaire, and seek direct entry to the examination.^{1,3} In the waiting room, ensure that the recommended distance between patients exists and they must be unaccompanied unless it is strictly unavoidable, ensure the use of facemasks everywhere and provide antibacterial gel based on 70% alcohol or facilitate hand washing to anyone who enters the department or stays in a waiting room, also ensure the use of masks for health personnel at the reception and consider plastic or acrylic barriers on the desks or receptions.^{11,14} The rescheduling will be done on a priority basis that relies mainly on clinical status and priority in the indication of each study, mainly when it is necessary change of guidance in the management, making a priority scale as shown in Table 1.

Transthoracic echocardiography in non-COVID-19 or non-suspected patients

The transthoracic echocardiogram remains the front-line study in the evaluation of patients with cardiovascular disease.^{11,14} Reprogramming will be done on a priority basis that relies on clinical status, when the indication is for follow-up, it is recommended to perform a limited echocardiographic study to resolve specific questions according to clinical suspicion or known heart disease, evaluating cardiac structures and their functionality to obtain the most relevant data for proper interpretation and decision making. They should always be performed by a certified echocardiographer, minimizing the need to repeat studies later,

limiting exposure time.^{5,15,16} The possibility of re-establishing the daily completion of all studies with their specific indications and in an extended manner should be evaluated as this pandemic develops, always assessing the risk of exposure of both personnel and patients.

Transesophageal echocardiogram

This echocardiographic modality implies a high risk of transmission because it is an aerosolgenerating procedure, requiring complete personal protection of the operators, as well as its execution in an exclusive area preferably, with space between patients of at least one hour that allows for adequate ventilation and subsequent sanitization. It is highly recommended to carry out screening tests for COVID-19 prior to performing a transesophageal echocardiogram when is available in non-urgent priority patients. In patients with a negative test, the high percentage of false negatives according the type of test available in each location should be considered, which in general is not negligible, so a strict use of full protective equipment is recommended, as well as for urgent studies in operating and intervention rooms where it is not feasible to wait for a test.^{11,15}

The clinical scenarios in which TEE cannot be postponed include: valve prosthesis dysfunction, cardiac masses, endocarditis and its complications (abscesses pseudoaneurysms and fistulae). It is also feasible to change to another imaging modality with less risk of exposure to contagion, such as in patients planned to undergo electrical cardioversion, where the TEE can be replaced by computed tomography to exclude the presence of thrombi in the left ear.^{2,8}

For patients who will require short-term treatment, always basing their careful indication on the clinical stage and improving their survival in the midst of the pandemic, the different cardiological societies are recommending opting for minimally invasive and short-stay procedures, such as structural interventions including mitral and tricuspid valve repair and left atrial appendage closure with percutaneous occlusion devices, where transesophageal echocardiography has taken a leading role, and its use will undoubtedly increase as this pandemic evolves.^{8,14,15}

Level of preference	Clinical status	Examples
High preference	Deterioration of functional class or new symptoms Initiation or monitoring of therapies	Dyspnea, chest pain, syncope, arrhythmias, related neurological disorder Start or follow-up chemotherapy
	Follow-up of recent or urgent preoperative procedures	After heart surgery and post-implantation of intracardiac ventricular pacing, IDC or post ventricular assist device in case of suspected complications Urgent preoperative in patients with functional limitations
Medium preference	Known asymptomatic heart disease requiring follow-up by progression	Cardiomyopathies Severe valve disease Pulmonary hypertension Structural post-intervention follow-up
	Monitoring of therapy employed	Therapy for pulmonary hypertension Heart transplant follow-up Ventricular assist devices monitoring in stable patients
	Non-urgent preoperative assessment	Priority but not urgent non-cardiac surgery
Low preference	Routine follow-up for chronic cardiopathy	Arterial hypertension Stable ischemic heart disease Periodic evaluation of valvular prosthesis
r	-	Stable ischemic heart disease

Table 1: Preferred indications according to clinical status for reprogramming studies.

Stress echocardiography

In a patient with suspected ischemic heart disease, stress echocardiography in its different modalities is an elective but essential examination for diagnosis. Exercise stress echocardiography (ESE) is a potential aerosol generating procedure due to the deep and rapid breathing generated during exercise, although the cycling protocol records fewer peak vents per minute, both should be avoided in the ascent and plateau phase of the pandemic; coronary CT angiography is preferred as an alternative for diagnosis when available.^{10,14} Any change of protocols should be evaluated by assessing each patient individually. Pharmacological stress echocardiography is a safer option, not considered as an aerosol generator and can be complemented with a careful clinical history and a questionnaire focused on assessing the functional capacity of the patient.^{11,13} When the performance of an ESE is strictly necessary it is recommended to previous perform SARS-CoV-2 PCR test, and examination should be

conducted in an exclusive area, with adequate ventilation with negative pressure if available, with automated blood pressure measurement and complete sanitation between each patients. Personal protective equipment is detailed in *Table 2*. The use of a surgical mask or face shield is recommended for patients.¹⁴

Echocardiograms in COVID-19 confirmed patients

Echocardiographic examination should generally be deferred in patients confirmed with COVID-19 as long as possible and there are no markers of myocardial damage. 20% of cases with SARS-CoV-2 disease present with elevated high-sensitive troponin T, brain natriuretic peptide type B (Pro-BNP) and D-dimer as markers of myocardial damage.^{11,17} Damage to the cardiovascular system has been documented by direct viral injury on ACE 2 receptors entering the myocardium and vascular endothelium which produces myocarditis and even vasculitis, microthrombosis and macrothrombosis

have been found in recent post-mortem studies, reporting important disruption in the coagulation and fibrinolytic system, with evidence of disseminated intravascular coagulation. The presence of acute coronary syndrome, as the first manifestation of infection by COVID-19, usually occurs in patients at high risk of coronary disease; its presence has also been noted in patients hospitalized for respiratory disease which suggests that the viral infection causes instability of atherosclerotic plaques, associated with an inflammatory response and cytokine storm with underlying endothelial dysfunction. Another documented mechanism is myocardial damage by hypoxia secondary to respiratory failure or septic status, observing an hyperinflammatory response observed in patients in advanced stages of the disease, demonstrated by elevation of biomarkers and cytokines such as IL-6, TNF-alpha, IL-2 R and ferritin, which are even considered of poor prognosis. Recently and in isolated cases, stress cardiomyopathy (tako-tsubo) has been reported, although the mechanism of viral action is not well established, but possibly associated with endothelial dysfunction, cytokine storm and an underlying catecholamine wave.¹⁸⁻²⁰

During the pandemic, COVID-19 cases will continue to be a daily challenge for echocardiography services. It is crucial to perform the echocardiographic evaluation in the shortest time possible, preferably in less than 10 minutes, using echocardiography machines exclusively for these patients, and to cover the equipment with plastic sleeves to facilitate subsequent disinfection, is important to remove from the equipment used the electrocardiographic cables and any other accessory that could favor cross contamination between patients and operators, resulting images should be recorded, use simultaneous multiplanar views, make the measurements off-line and it is recommended to use even automated tools based on image recognition in the opinion of the operator, with the aim of reducing acquisition times of examination as part of a modified focused protocol.^{2,3,14} In the prone patient, consider as the only available apical 4-chamber view, and point it out in the echocardiographic report; recently Marvaki and collaborators have published a small work where it is proposed as an alternative to use the transesophageal transducer in pronounced and intubated patients in intensive care to obtain transthoracic images with results comparable or superior to the conventional transthoracic route with the advantage of acquiring multiplanar images of diagnostic quality but the disadvantage of requiring two operators for their acquisition.²¹ The main indications for TTE in patients confirmed with SARS-CoV-2 include: assessment of hemodynamic parameters up to 29% of cases and in those with major associated adverse cardiovascular events such as pulmonary embolism, heart failure, elevated biomarkers, acute coronary syndrome and myocarditis (up to 46%), the rest of the indications range from previous known heart disease, associated endocarditis, arrhythmias and cardioembolic events.¹⁷ The focused protocol POCUS (Point

Table 2: Personal protective equipment according to risk of exposure from the echocardiographic study				
Intermediate risk (dropwise)	Transthoracic echocardiography/ pharmacological stress echocardiography	Surgical mask Face shield Cloth or disposable gown Gloves		
High risk (by aerosols)	Transesophageal echocardiogram, stress with exercise	Face shield or protective glasses or goggles Mask with filter class N95 or higher Hat or diving suit Disposable waterproof gown or coverall Boots or shoe covers Double pair of gloves		

of care ultrasound) includes cardiac, pulmonary and vascular approaches, whose main indication and utility is widely demonstrated in the critical patient with hemodynamic instability, employing apical views, short and long parasternal axes as well as subcostal view, evaluating the following structures:

- Left ventricle: evaluate dimensions, global and segmental contractility to rule out myocarditis, acute ischemic coronary syndrome or cardiomyopathy.
- Right ventricle: evaluate dimensions and rule out dysfunction data.
- Valves: to evaluate the presence of regurgitation or stenosis and its degree of severity, to rule out pre-existing valve disease or acute dysfunction. Emphatically evaluate the presence or not of peak tricuspid regurgitation gradient with the intention of evaluating the possibility of elevated of pulmonary systolic pressure and estimate its value.
- Pericardium: to establish the presence of pericardial effusion and its hemodynamic repercusion.

The pulmonary echo approach will be performed by personnel trained in the technique, assessing the anterior, lateral and posterior areas of both lungs to rule out B lines, subpleural or pulmonary consolidation, pleural thickening or pleural effusion to differentiate pulmonary congestion of cardiac origin or parenchymal pulmonary involvement. The ultrasonographic vascular examination includes the evaluation of the inferior vena cava in subcostal view and/ or the assessment of the jugular venous pulse to determine the blood volume status and an assessment of the venous system of the lower limbs, if there is a clinical suspicion of injury at this level, mainly to rule out deep vein thrombosis.^{11,16} Recent studies have shown that a modified focused protocol, despite being acquired in a short time, achieves adequate diagnostic accuracy in up to 70-80% of cases and allows for rapid decision making in respiratory triage and identification of those patients requiring extended echocardiographic evaluation at a later date.^{15,17} Echocardiographic findings in patients having COVID-19 have been described in studies with different designs, most with a small number of patients, however some of these findings have statistical significance as well as clinical and prognostic relevance. Right ventricular dilation with or without dysfunction is the most frequent echocardiographic abnormality found in 32 to 39% in different series, without finding significant differences in major comorbidities (diabetes, hypertension and known coronary heart disease). The physiopathological mechanism seems to be multifactorial including increased resistance and pulmonary pressures secondary to hypoxic vasoconstriction, thrombotic events, cytokine damage and direct viral injury. Right ventricular dilatation defined as a basal diameter greater than 41 mm measured in right ventricle focused apical 4-chamber view or a VD:VI ratio > 0.9is strongly associated with increased hospital mortality in patients with VOC-19 (Figure 1).²² In addition to hypoxic vasoconstriction, right ventricular dysfunction is due to decreased lung volume, excessive positive pressure at the end of expiration, pneumonia, hypercapnia and the effect of alpha-agonist drugs. The frequently documented parameters of right ventricular dysfunction are: fractional area change, TAPSE, tricuspid lateral anular systolic tissue velocities (S') and decreased values of free wall strain values and have been recognized as independent predictors of mortality with statistical significance (p < 0.001), with the advantage for the 2D non Doppler strain (speckle tracking) of being angle independent in its acquisition, which positions it as the best tool to evaluate



Figure 1: Right ventricle focused apical 4-chamber view with right ventricular dilation in a patient with COVID-19. Courtesy: Dr. Juan A Calderón González.



Figure 2: Shortened pulmonary flow acceleration time in a patient with COVID-19. Courtesy: Dr. Alejandra Guzmán Ayón.

the right ventricular function demonstrated by Li and collaborators in a recently published study with a limited number of patients that established a cut-off value of less than -23% with a sensitivity and specificity of 94.4 and 64.7% respectively; however it will require further validation in future multicenter studies and with a larger number of patients. So far the recommendation is to combine the available parameters to determine right ventricular dysfunction.²³ A shortened pulmonary flow acceleration time (Figure 2) or the presence of a high peak tricuspid regurgitation gradient as a result of increased pulmonary pressure or pulmonary vascular resistance in the various series has also been documented. The presence of acute severe right ventricular dysfunction should also rise suspicion to rule out the presence of peripheral venous thromboembolism associated with pulmonary thromboembolism or even microvascular thrombosis, where paradoxical septal movement is often observed causing left ventricular D-shape morphology secondary to pressure overload, further contributing to the drop in cardiac output and blood pressure (Figure 3). The peak tricuspid regurgitation gradient is a difficult parameter to acquire in the critical patient and its has been reported as impossible to obtain an adecuate spectrum to estimate the systolic pulmonary pressure in up to 65% in small studies. All the above point out that the evaluation of right ventricular dysfunction by echocardiography is essential for risk stratification in these patients. Left ventricular

systolic dysfunction has been associated with cytokine storm damage, being documented in only about 10% of cases and presenting in patients having troponin elevation > 50 ng/Lup to 46%, a little less than half of patients with left ventricular dysfunction present regional wall motion anormalities secondary to micro or macrovascular ischemic heart disease or stress cardiomyopathy associated with COVID-19 infection. Diastolic dysfunction is documented in up to 16% of patients that have varying degrees of elevation of filling pressures, even without data on left ventricular dysfunction. Valvular alteration and other findings occur in a non-significant percentage.¹⁷ Indications for a follow-up echocardiogram in patients having COVID-19 are mainly due to hemodynamic instability, cardiac deterioration, or progression of respiratory failure, and the most frequent finding is progressive decline of right ventricular function, due to the progression of lung damage by the mechanisms described above, and also in many cases due to microthrombosis or major vascular occlusion with D-dimer and fibrinogen elevation, associated or not with deep vein thrombosis, reported with high incidence in hospitalized patients suffering from COVID-19 infection.^{19,20}

In patients recovering from COVID who require an echocardiogram on an outpatient basis, the indication should be based on the priorization of the examination, preferably requesting a negative test beforehand. If it is not available, try to perform the examination



Figure 3: Short axis parasternal with left ventricular D-shape in a patient with COVID-19. Courtesy: Dr. Juan A. Calderón González.

in a designated area, after adequate sanitation, facilitating the least contact of the patient with other patients and medical staff, minimizing the circulation of personnel with subsequent strict sanitation and ventilation of the area and any equipment used, including hallways and bathrooms, in coordination with institutional cleaning and hygiene services, both for positive cases with active disease and for recovering patients who access the echocardiographic departament.¹³

Personal protection measures and equipment

Adequate hand washing or disinfection with 70% alcohol-based antibacterial gel frequently and between patients remains the cornerstone of protection against virus transmission and should be equally strict in the period of reintroduction of services, it is recommended to adhere to the use of personal protective equipment according to the degree and nature of exposure and the degree of risk of the examination, exposure to drops and/or aerosols and whether the study is intermediate or highrisk as shown in Table 2, as well as maintaining distance between personnel and minimizing the risk of exposure to physicians in training and non-essential personnel. However, as this pandemic develops, measures to ensure reintegration into their face-to-face training program or hybrid approach should be reassessed, taking into account virtual teaching methods. Healthcare workers in vulnerable conditions, such as: those over 60 years of age, immunosuppressed, pregnant women, and other recognized comorbidities at risk in the pandemic, should be considered to avoid performing the highest risk procedures. Relaxation of protective measures will depend on many factors, including the prevalence and incidence of COVID-19 cases, at each facility and in the locality, including institutional policies.

Disinfection of equipment and designated areas

Likewise, it is imperative to carry out schedule sanitization with appropriate viricidal agents in waiting rooms, frequent disinfection of surfaces and floors, and to facilitate ventilation of all areas.⁵ Disinfection of the equipment used

with compatible solutions should be conducted by consulting the supplier's manual for each specific machine. It is recommended that the equipment be covered with plastic sleeves that allows handling of the probes and keyboard, thus facilitating disinfection with any sanitizing solutions, between one patient and another, in addition to better preserving the equipment.^{5,8} The cubicles for examination execution areas should be sanitized in a meticulous and frequent manner, respecting the time between studies to facilitate ventilation, include examination couches and extend it periodically to the interpretation offices or meeting rooms.^{13,24}

Reintroduction of teaching or training programs

Students should continue to be excluded from high-risk areas until determined by the appropriate academic authorities; residents and fellows in training may be reinstated in a gradual manner that minimizes exposure and should not participate in examinations of confirmed COVID-19 patients of recovering ones without a negative test, facilitate and emphasize the use of personal protection equipament and hygiene measures and equipment at all times.^{3,14} Continue or resume remote academic sessions using videoconference and reassess as this pandemic evolves.^{11,13}

CONCLUSIONS

The challenge continues with the reincorporation of all the cardiological departaments in the middle of the pandemic as phases, in the echocardiographic departament the classical indications of the different examinations will be gradually taken up again according to the prevalence of the disease by COVID-19 in each location and the degree of immunity of the population, with the same consideration for the use of personal protective equipment. The final objective will always be to try to offer a timely and effective care to cardiovascular diseases with any necessary protective measures to avoid viral transmission to patients and medical staff. Immersed in this objective, doctors will continue to attend to patients with COVID-19 in whom the echocardiographic findings so far point out of image modality as an invaluable tool in initial assessment and follow-up, allowing a better hemodynamic evaluation that can, if necessary, dictate management adjustment or be used as a examination with prognostic value. It is still uncertain whether the change in the daily operation protocols to which medical professionals have been accustomed for several decades will be permanent, this will be determined by the prevalence of the disease, as well as by the guidelines that will provide future evidencebased research on the COVID-19 and SARS-CoV-2 spectrum. Based on this, it is important to emphasize that these recommendations may be dynamic in the future.

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Anexo 1: Symptom Questionnaire.				
Name: Age:		Date:		
		Gender:		
1. Have you had any of the	ne following (ma	ajor) signs or symptoms in the last 10 days?		
Cough	Yes	No		
Fever	Yes	No		
Shortness of breath*	Yes	No		
* Serious detail				
Headache*	Yes	No		
* Consider irritability i	n < 5 years			
2. Have you also had any	of the following	g (minor) signs or symptoms?		
Muscle or joint pain	Yes	No		
Conjunctivitis	Yes	No		
Runny nose	Yes	No		
Sore Throat	Yes	No		
Chest pain	Yes	No		
Shivers	Yes	No		
Loss of smell	Yes	No		
Loss of taste	Yes	No		
	Yes	No		
3. Have you been in direc	t contact with a	confirmed COVID-19 in the last two weeks?		

Anexo 1: Symptom Questionnaire.

If you responded to at least one of the major signs or symptoms and accompanied by one of the minor signs or symptoms, it is considered a **suspicious case**.

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