CONSENSUS STATEMENT

Key issues in emergency department management of COVID-19: proposals for improving care for patients in Latin America

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The incidence of the coronavirus disease 2019 (COVID-19) in Latin America and Spain and its impact particularly on hospital emergency departments have been great, sustained, and unpredictable. Unfortunately, this situation will continue in the medium term, regardless of the diverse concepts and definitions used to identify cases or hypotheses about the role of staff. In the context of the worldwide pandemic, a multinational group of experts from the Latin American Working Group to Improve Care for Patients With Infection (GT-LATINFURG) has drafted various opinion papers for use by emergency care systems in the member countries. The GT-LATINFURG is comprised of representatives from the 13 scientific associations affiliated with the Latin American Federation for Emergency Medicine (FLAME). Experts from the Spanish Society of Emergency Medicine (SEMES) also participated. The present consensus statement offers protocols and recommendations to facilitate the work of hospital emergency departments with regard to key issues the group identified, namely, the need for reorganization, triage, and routine test availability. Additional issues discussed include biomarkers; clinical, laboratory, radiologic, and microbiologic criteria for identifying patients with COVID-19; and risk and prognostic factors for mortality that emergency staff can use to quickly detect severe cases in our settings.

Keywords: Emergency department. COVID-19. Pandemics. Epidemiology. Diagnosis. Clinical Characteristics. Biological markers. Quality improvement strategies.

Puntos clave sobre la covid-19 en los servicios de urgencias: propuestas de mejora para su atención en Latinoamérica

La incidencia y el impacto de la COVID-19 (Coronavirus Disease 2019) en Latinoamérica y España, en particular en sus servicios de urgencias hospitalarios (SUH), independientemente de la diversidad de los conceptos y definiciones de casos confirmados o sospechosos empleados ha sido, es, y, desgraciadamente a medio plazo, va a seguir siendo enorme, sostenida e imprevisible. En este escenario global, un grupo multinacional de expertos y representantes del Grupo de Trabajo Latinoamericano para la mejora de la atención del paciente con Infección en Urgencias (GT-LATINFURG), compuesto por 13 Sociedades y Asociaciones Científicas que integran la Federación Latinoamericana de Medicina de Emergencias (FLAME), junto con la Sociedad Española de Medicina de Urgencias y Emergencias (SEMES), ha elaborado diversos documentos técnicos y de opinión destinados a los profesionales de los Sistemas de Urgencias y Emergencias de nuestros países. El objetivo de este artículo es ofrecer unas pautas o recomendaciones consensuadas para facilitar la actuación de los SUH en relación los puntos que los miembros del grupo han considerado más interesantes o clave en relación a: la necesidad de reorganizar los SUH, triaje, disponibilidad de pruebas complementarias habituales y otras como biomarcadores, la identificación del paciente con COVID-19 a través de criterios clínicos, analíticos, radiológicos y microbiológicos, así como factores de riesgo, pronóstico y de mortalidad que puedan ayudar

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a detectar rápidamente a los pacientes graves a su llegada a los dispositivos de Urgencias y Emergencias de los hospitales en nuestro entorno.

Palabras clave: Servicio de Urgencias. COVID-19. Pandemia. Epidemiología. Diagnóstico. Características clínicas. Biomarcadores. Estrategias de mejora.

COVID-19: the pandemic of the 21st century

On December 31, 2019, the Wuhan Municipal Health and Sanitation Commission (Hubei Province, China) reported a cluster of 27 cases of pneumonia of unknown etiology. Seven of them were severe, with onset of symptoms detected in early December 2019[1,2]. One week later, January 7, 2020, a new type of virus of the *Coronaviridae* family was identified as the causative agent of the outbreak and was named "new coronavirus" or "2019-nCoV". Subsequently, the virus was named SARS-CoV-2 (Severe Acute Respiratory Syndrome COronaVirus 2), and the disease was named COVID-19 (Coronavirus Disease 2019). The genetic sequence of the virus was shared by Chinese authorities on January 12[3,4]. A day later, a case of COVID-19 was confirmed in Thailand, the first outside of China[5]. Given the impact that COVID-19 was having in China and Southeast Asia, the World Health Organization (WHO) declared the SARS-CoV-2 outbreak a "Public Health Emergency of International Concern (PHEIC)" on January 30. This was the sixth time that WHO declared a PHEIC since 2005[4]. On March 11, 2020, WHO, concerned by the alarming levels of spread of the disease and its severity, and by the alarming inaction and lack of response in taking preventive measures in different countries with community transmission, determined that COVID-19 should be characterized as a global and severe PANDEMIC[4,5].

The impact by country and continent during 2020 has been very different, intensifying in China and the northern hemisphere during February, March and April 2020 and increasing exponentially in Central and South America in May, June and July 2020[5-7].

COVID-19 is a zoonosis. Phylogenetic analyses have identified the bat as a reservoir (96% similarity with a SARS-like coronavirus strain -BatCov RaTG13-, isolated in bats). Other intermediate hosts have yet to be identified and confirmed[3,9].

For the third time in the last 2 decades a zoonotic coronavirus has jumped to humans and has demonstrated the ability to thrive in our species. Although we knew and identified 2 alpha coronaviruses (HCoV-229E and HCoV-NL63) and 2 beta coronaviruses (HCoV-HKU1 and HCoV-OC43) as pathogens responsible for more banal clinical pictures in humans, in 2002 a fifth coronavirus emerged that caused SARS (severe acute respiratory syndrome), which affected more than 8,000 people in 32 countries and had a lethality of 10%[9-11]. This virus was transmitted from the horseshoe bat, via animal intermediaries such as civets to humans, and subsequently by the airborne route from person to person[3].

In 2012, the Respiratory Syndrome Coronavirus (MERS-CoV) was identified and defined in Saudi Arabia that used camelids to reach humans, and subsequently could be transmitted from person to person. With 2,516 cases, the case fatality of this sixth coronavirus was much higher, at 35%, although fortunately it was limited to 2,516 cases in 27 localized countries[9-11] (Figure 1).

Current scenario and objectives of the study

During this complicated moment in history and in a global scenario for all humanity, the Latin American Working Group for the improvement of the care of patients with infection in the emergency department (GT-LATINFURG) began its work a little over 3 years ago. The aim was to promote and develop organizational, diagnostic-therapeutic recommendations and strategies to optimize and facilitate the management of patients with severe infection in the emergency department12. In November 2019, in Toledo (Spain), after the signing of an ambitious collaboration agreement between FLAME (Latin American Federation of Emergency Medicine) and SEMES (Spanish Society of Emergency Medicine), this GT was formalized and extended its representation to the 14 Societies and Scientific Associations that make up FLAME together with SEMES.

Since then, the GT-LATINFURG, aware of the severity and importance for the whole world of the pandemic caused by the new SARS-CoV-2 coronavirus (COVID-19), has produced several technical and opinion documents for emergency professionals in our countries[12,13]. With the most up-to-date scientific and institutional information (which should be constantly reviewed), this expert document is intended as an additional tool to assist in decision making during the care of adult patients with COVID-19 in the hospital emergency department (ED). Although the consensus is based on the most recent published evidence available on the subject, it is not mandatory and does not replace the clinical judgment of the ED physician in each particular case or the official regulations and instructions in each country or geographic region.

The objectives of this consensus document (CD) are as follows:

1. To review, analyze and compare the current situation of the key points and most relevant problems in the care of patients with COVID-19, in the opinion of the authors, in the EDs of several Latin American countries.
2. To issue several recommendations and proposals that could be implemented in the EDs of the countries

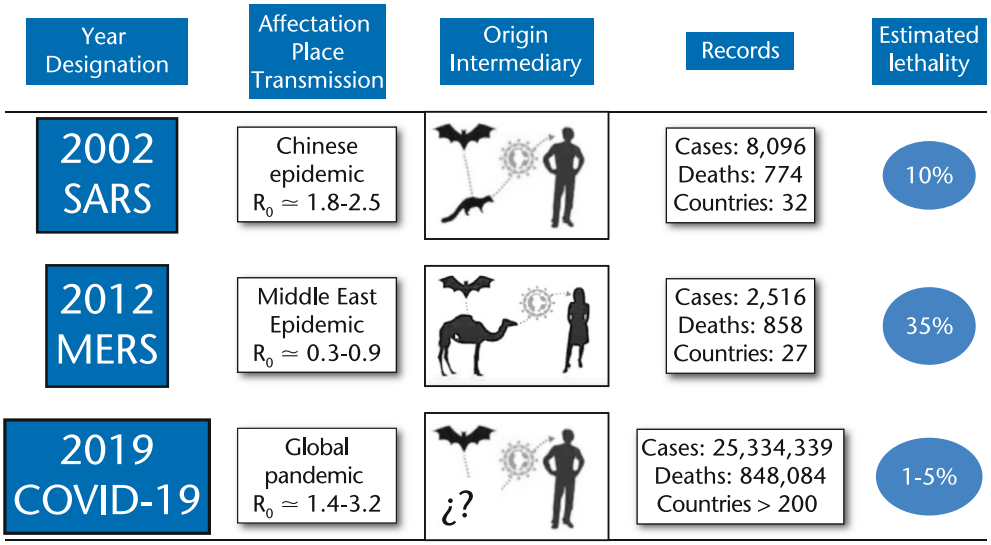

Figure 1. Severe human coronavirus infections in the 21st century.
*Data as of September 1, 2020. R_0 = basic reproductive number.
Source: Compiled by the authors.

represented in the GT-LATINFURG (without interfering with the regulations of each country, but being complementary).

Method

A team of 20 specialists in Emergency Medicine with special links and dedication (designated by FLAME and SEMES) in the field of infectious diseases and working groups related to infectious processes and COVID-19, belonging to the GT-LATINFURG, participated in the preparation of this CD.

The phases for the preparation of this article were:

First, a literature and document search was conducted that included 2 parallel and bounded strategies between January 1, 2020, and August 20, 2020:

1) Bibliographic search in the main databases, generic internet search engines, and health funders were conducted. Priority was given to Systematic Reviews (SR), health technology assessments (HTA), economic evaluations (EA), clinical practice guidelines (CPG), coverage policies (CP) of different health systems, randomized clinical trials (RCT), and observational studies, until August 2020 without any language restriction. The identification of the different studies was carried out by means of an exhaustive systematic search of the scientific literature in the following databases: MEDLINE (PubMed), TRIP database (TRIP: Turning Research Into Practice), The Cochrane Library, CRDYork (Centre for Reviews and DisseminationUniversity of York), Epistemonikos, BRISA (Regional Database of Health Technology Assessment Reports of the Americas), LILACS (Latin American and Caribbean Health Sciences Literature), INAHTA (The International Network of Agencies for Health Technology Assessment), PROSPERO (International prospective register of systematic reviews), IECS (Institute for Clinical Health Effectiveness), NIHR (National Institute for Health Research), BMJ (British Medical Journal), CINAHL (Cumulative Index to Nursing and Allied Health Literature), EMBASE (Excerpta Medica Data Base). Using the following keywords (and combinations thereof): "novel corona", "coronovirus", "coronavirus", "corono virus", "covid-19", "2019-nCoV", "sars-cov-2", "severe acute respiratory syndrome", "Acute respiratory distress syndrome", "Pandemic", "Epidemiology", "Diagnosis", "Treatment", "Clinical characteristics", "Biological markers", "mortality", "mechanical ventilation", "Healthcare Professionals", "Health Care Personnel", "healthcare workers", "Efficacy", "Safety", "Anticoagulation", and "Antibiotics".

2) Local publications, registries, official data obtained from public administrations or governments and selected relevant and recent articles from different biomedical journals chosen by the authors in 2 languages: Spanish and English.

Secondly, after reading all the documents selected by the authors, the key points and most relevant problems related to the care of adult patients with suspected or confirmed SARS-CoV-2 infection (COVID-19) in the ED were decided and agreed upon (Table 1). Always from the common perspective and basic aspects that could be useful for most centers and countries, assuming the evident diversity of scenarios, resources, epidemiological and socio-political situations, etc. Due to the limitation and objectives of this article, it was decided that some important points that were already recently updated by the GT-LATINFURG (August 2020) would not be developed in it in order not to be repetitive. So for them [management and treatment schemes (antiviral, anti-inflammatory and antibacterial if applicable), ventilatory and hemodynamic support, cardiopulmonary resuscitation, protective measures for health-

Table 1. Decalogue of key points and recommendations in the care of the adult patient with suspected or confirmed COVID-19 in the ED

1. Impact and evolution of the COVID-19 pandemic in Latin America and Spain.
2. Case definitions and concepts of SARS-CoV-2 infection.
3. Recommendations for the reorganization of the ED to face the pandemic.
4. Complementary tests available and recommended in the ED in the patient with COVID-19.
5. Identification of the patient with COVID-19 in the ED: clinical criteria.
6. Identifying the patient with COVID-19 in the ED: analytical criteria.
7. Identification of the patient with COVID-19 in the ED: radiologic criteria.
8. Identification of the patient with COVID-19 in the ED: microbiologic criteria.
9. Risk factors, admission, severity, and mortality of patients with COVID-19.
10. Role of biomarkers of inflammation and infection as a tool to aid in the diagnosis and prognostic assessment of patients with COVID-19.

ED: hospital emergency department.

care personnel, criteria and indications for admission to hospital and intensive care medicine, among others] the reader is referred for consultation to these publications on the FLAME and INFURG-SEMES websites:

– Update of the Recommendations for Action in Cases of Infection with the New Coronavirus (SARS-CoV-2). Second Document August 2020 at: http://flameoficial.com/actualizaciondelasrecomendacionesdeactuacionfrenteacasosdeinfeccionporelnuevocoronavirussarscov2/.
– Clinical Guide 2020 on antibiotherapy for pneumonia in patients with COVID-19 and pharmacological interactions between antibiotics and drugs for the treatment of SARS-CoV-2 at http://www.infurgsemes.org.

And finally, thirdly, with the agreement of all the authors, the CD was prepared with the proposals, strategies and recommendations to be adopted by the hospitals, health systems or competent administrations.

Results

Impact and development of the COVID-19 pandemic in Latin America and Spain

In Spain, the first case was officially reported on January 31, 2020; subsequently, during the months of February and March, confirmation was reported in the different Latin American countries (Table 2)[13,14].

Affectation by country and continent during 2020 has been very different, intensifying in China and the northern hemisphere during February, March and April 2020, and increasing exponentially in Central and South America in May, June and July 2020[5-7]. In August 2020, the pandemic continues to progress, especially in the USA and Latin America (53% of the new cases registered in the week of 13-20 August 2020 worldwide)[6], without achieving control of the first wave and, in some countries, such as Spain, a second wave with a less pronounced slope but with an uncertain trend is already underway[8].

Table 2. Dates of the first confirmed case of COVID-19 in different Latin American countries and Spain

January 21, 2020 in the United States of America.
January 31, 2020 in Spain.
February 26, 2020 in Brazil.
February 28, 2020 in Mexico.
February 29, 2020 in Ecuador.
March 1, 2020 in Argentina and the Dominican Republic.
March 3, 2020 in Chile.
March 6, 2020 in Peru, Colombia and Costa Rica.
March 7, 2020 in Paraguay.
March 13, 2020 in Venezuela.
March 18, 2020 in El Salvador and Nicaragua.

Source: References 4 and 13.

As of September 1, 2020, 25,334,339 cases have been officially reported in more than 200 countries or geographic regions in the world, with an approximate rate of 190,000 new cases per day. And a total of 848,084 deaths (about 6,500 per day)[6] had been recorded[6]. All of them confirmed by PCR (polymerase chain reaction), although the real estimate of unconfirmed cases would multiply these figures by an unknown number of cases and deaths. The 10 countries in the world with the most confirmed cases are: USA (6,118,204), Brazil (3,908,272), India (3,691,166), Russia (1,000,048), Peru (652,037), South Africa (627,041), Colombia (615,168), Mexico (599,560), Spain (470,973) and Argentina (417,722)[6]. Table 3 shows the comparative count of registered cases and deaths due to COVID-19 in the world, in different Latin American countries and in Spain. Figure 2 shows a synoptic map showing the cases registered per million in-

Table 3. Registered cases and mortality up to September 1, 2020 due to COVID-19 in different countries of the Americas and Spain

	Confirmed cases	Cases/ 1,000,000 people	Deaths	Fatality rate*
Worldwide total	**25,334,339**	**3,258**	**848,084**	**3.35%**
United States	6,118,204	18,565	186,348	3.05%
Argentina	417,722	9,295	8,660	2.07%
Brazil	3,908,272	18,493	121,381	3.11%
Colombia	615,168	12,454	19,663	3.20%
Costa Rica	41,287	8,163	436	1.06%
Chile	413,145	21,622	11,321	2.74%
Ecuador	114,309	6,548	6,571	5.75%
El Salvador	25,820	3,981	724	2.80%
Spain	470,973	9,999	29,152	6.19%
Mexico	599,560	4,737	64,424	10.75%
Nicaragua	4,494	696	137	3.05%
Paraguay	17,662	2,469	326	1.85%
Peru	652,037	20,293	28,944	4.44%
Dominican Republic	94,979	9,169	1,738	1.83%
Venezuela	46,728	1,450	386	0.83%

Source: References 6, 8 and 13.
*Fatality rate: quotient between the number of deaths due to COVID-19 and the number of persons diagnosed with COVID-19 until September 1, 2020.

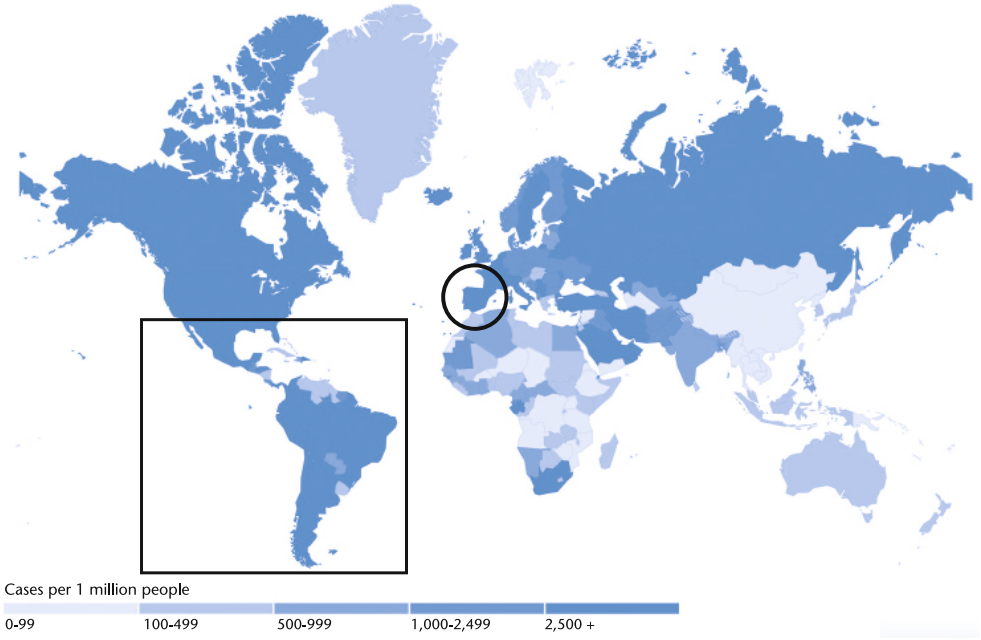

Figure 2. Worldwide representation of the rate of affected persons per million inhabitants. Source: references 6 and 11. Simulation of the situation on September 1, 2020.

habitants in the different countries and regions of the world. At that time, the COVID-19 determined a global lethality of 3.3% (between 110% depending on the different countries and moments in the evolution of the pandemic)[6,11]. This depends on many factors and cannot be directly compared between countries, as there are decisive differences in the definitions and ways of counting the number of patients who died[13-15]. Table 3 shows the lethalities resulting from the official cases and deaths in our countries.

One of the fundamental characteristics of the enormous impact of the COVID-19 pandemic is its high transmission capacity. This is usually estimated on the basis of the so-called basic reproductive number (R_0), which is the average number of secondary cases produced from one case and varies proportionally according to social contacts. A value of $R_0 < 1$ indicates a low capacity for the spread of an infectious disease, while values of $R_0 > 1$ indicate the need to employ control measures to limit its spread[10,11]. Thus, reliable estimates place the R0 value of COVID-19 between 1.4 and 3.2 in the initial months of the pandemic (although 2 recent reviews include different studies that establish it between 1.5 and 6.1), similar to the R0 of SARS coronavirus at the beginning of the epidemic, which was reduced to an R_0 of 0.67 to 1.23 at the end of the epidemic. In contrast, MERS coronavirus had always maintained lower R0 values (0.29 to 0.89)[10,11]. This explains, despite the different lethalities shown in Figure 1, the limited impact of the SARS and MERS coronavirus epidemics. Meanwhile, after more than 8 months of global involvement by COVID-19, there are countries and regions with $R_0 < 1$ (in which the epidemic curve trend has been contained and changed) and others where the spread continues to increase with $R_0 > 1$-2[11,12,16].

Regrettably, after 8 months of struggling against SARS-CoV-2, the most powerful weapons continue to be responsibility, preventive measures (mask, hand hygiene and adequate protection, social distance) and the help of management, treatments and support, which we have learned "blindly" so far in 2020.

Case definitions and concepts of SARS-CoV-2 infection

Although in the first weeks of the pandemic the WHO indicated criteria for defining "suspected case", "confirmed case", "close contact", "case under investigation", "death due to COVID-19", among other concepts, almost from the beginning of the pandemic each country has applied its own criteria and definitions adapted to its epidemiological and sociocultural situation and as indicated by its own Ministries of Health or Health[13]. These concepts have also changed on many occasions during these 8 months of 2020[5,15]. The definitions and concepts, as well as the changes they have undergone in Latin America and Spain, can be consulted and compared in previous publications of the GT-LATINFURG (Update of the Recommendations for action in cases of infection by the New Coronavirus-SARS-CoV-2. Second CD of August 2020)[13].

This disparity of concepts has made it impossible to correctly compare the incidence, impact and lethality among countries and regions of the world. This, in turn, makes it impossible to know exactly how the pandemic affected the first 8, which is vital information for preparing correctly and focusing more adequately, without making the same mistakes again, in the coming months until it can be considered to be under control[13,15,20]. It is also important to place each region or

country in a specific epidemiological situation. The WHO has defined 4 scenarios of COVID-19 transmission[15]:

– Absence of cases: countries/territories/areas with no cases.
– Sporadic cases: countries/territories/areas with one or more cases, imported or locally detected.
– Clustering of cases: countries/territories/areas with cases clustered by time, geographic location and/or common exposure.
– Community transmission: countries/territories/areas with larger outbreaks of local transmission, defined by an assessment of factors including: 1) large number of cases unrelated to chains of transmission, 2) large number of cases detected by sentinel laboratory surveillance or by the largest number of positive tests on sentinel specimens (routine testing of respiratory secretions in established laboratories), 3) multiple clusters of unrelated cases in various sectors of the country/territory/area.

Countries may have one or more of these scenarios at a sub-national level and should adapt and adjust their approach to the local context. On the other hand, they can also move in both directions between transmission scenarios, so that, for example, the "no cases" scenario includes both countries that have never had any cases of COVID-19 and those that have had cases but at the time the scenario is defined have no cases[13,15,20].

As of September 1, 2020, all GT-LATINFURG member countries have community transmission (Spain, with more than 1,200 active outbreaks, is the European country with the highest number of new cases in the month of August)[6,8].

Recommendations for reorganization of hospital emergency departments to cope with the pandemic

It is very important to establish 2 differentiated and separate circuits from the time patients enter the ED to ensure that patients with COVID-19 do not come into contact with other patients who are in the ED or are admitted to the ED[15]. Although this measure could be controversial, especially when there is high community transmission, and it is difficult to establish which patients should remain in one or the other circuit (due to the unspecificity of the symptoms and the subsequent confirmation of COVID-19 in patients not initially suspected), we believe that it is necessary and can prevent transmission between patients and ED staff. The principles to be followed should be: identify, isolate and report. Ideally, 2 separate ED admissions should be enabled, one for patients with respiratory pathology or suspected of having COVID-19 and another for the rest of the reasons for consultation. The admission and triage system should also be different for each circuit[21].

Visual information (posters, leaflets, etc.) should be posted in strategic places to provide patients with instructions on hand hygiene, respiratory hygiene and coughing. It is also recommended that dispensers with hydroalcoholic solution be available within reach of patients and staff, and that surgical masks be offered to those who come with symptoms of acute respiratory infection[13,15,21].

The identification procedure should begin as soon as the first contact is made with the patients attending the ED. Depending on the characteristics of the patients, this can occur in the administrative area of the admitting service or in triage or even at the very entrance to the hospital (to the ED)[13,21].

If the first contact occurs in the admission area, and considering that it involves personnel from outside the health system, the questions will be limited to the epidemiological criterion. If this is positive, the patient will be referred to the isolation circuit in order to avoid contact with people being treated in the conventional circuit, thus avoiding unnecessary exposure[13,21]. The personnel transferring the patient to the isolation circuit will wear surgical masks and gloves. If the epidemiological criterion is positive, the patient will be invited to put on a surgical-type mask and to wash hands with hydroalcoholic solution.

Once in the isolation circuit, the healthcare personnel can complete the triage and anamnesis to verify that the patient meets the epidemiological and clinical criteria. Unlike the previous case, identification should be complete and based on both epidemiological and clinical definition, inquiring about the presence of symptoms of viral infection or respiratory symptoms and recent travel to risk areas or contact with COVID-19 cases (according to the corresponding epidemiological scenario)[13,15,21]. If the case is detected in triage, the patient will be invited to put on a surgical-type mask and perform hand washing with hydroalcoholic solution and will be transferred to the ED isolation circuit[13,15,21].

Once the patient is in the isolation circuit, an anamnesis will be performed with special emphasis on clinical assessment and epidemiological history (specific dates, risk exposures, etc.). If the patient meets the criteria of a "case under investigation", the corresponding public health agency will be notified[13,15,21]. The patient's relatives or companions should not enter the isolation circuit, and they will be informed of the procedure to be followed. In the case of minors or patients requiring accompaniment, the necessary measures should be adopted for their protection through the use of appropriate personal protective equipment[13,15,21].

In areas where there is community transmission of the virus, two different care circuits should be permanently established from the outset, enabling 2 different ED admissions, one for patients with respiratory pathology and/or suspicion of COVID-19 and another for the rest of the reasons for consultation. The admission and triage should also be different for each circuit[13,15,21].

Signs should be posted outside the hospital to indicate the appropriate entrance door for patients, directing those with fever, cough or shortness of breath to the entrance of the isolation circuit, in addition to the clinical criteria established by the ED itself. Both in con-

Table 4. Complementary tests to be performed in patients with COVID-19

GENERAL ANALYTICS: ("COVID-19 profile")

Depending on the estimated clinical severity, the epidemiological situation in each region or country, as well as the availability of tests to be performed in the hospital emergency department (ED), it is advisable to analyze the following determinations in a patient with suspected COVID-19[7,13,14,14,22,23]:

- Hemogram with cell count and coagulation study, fibrinogen, fibrinogen degradation products (FDP), D-dimer and ferritin.
- Basic biochemistry with glucose, ions, urea, creatinine, uric acid, lactate dehydrogenase (LDH), alkaline phosphatase (ALP), gamma glutamyl transpeptidase (GGT), aspartate aminotransferase (AST or GOT), alanine aminotransferase (ATL or GPT) and direct and total bilirubin. Additionally, if available, complete the study with: triglycerides, calcium, albumin, total proteins, creatine phosphokinase (CPK) and troponin.
- Arterial blood gases (when deemed necessary by the clinical situation or characteristics of the patient, if respiratory rate ≥ 22/minute or if O_2 saturation assessment by pulse oximetry ≤ 93%).
- Lactate, C-reactive protein (CRP) and procalcitonin (PCT). Assess, if available, perform proadrenomedullin (proADM) and/or suPAR (soluble urokinase-type plasminogen.

IMAGING STUDIES:

Request posteroanterior chest radiography (CR) (and lateral if respiratory symptoms are evident). Consider performing a portable X-ray depending on the need for isolation and risk of contagion to others in the ED. It is recommended for all patients diagnosed microbiologically or with suspected COVID-19 if the clinical situation demands it (respiratory symptoms), provided that there is no clear contraindication or the particular situation does not recommend it)[22]. Even in asymptomatic or oligosymptomatic patients, both in adults and children, a high percentage of radiological pulmonary alterations, such as multifocal opacities, have been found in up to 70% of cases[23-25]. However, its diagnostic yield in the initial stages of the disease is limited (< 60%), since pathological findings that are identifiable on chest computed tomography (CT) may not be detected[26,27]. This fact, together with the initial circumstances of the pandemic, when the accumulation of suspected cases exceeded the availability of microbiology tests, led certain working groups to adopt TCT as a diagnostic test in the absence of available microbiology tests. TCT obtained very good results in these studies, showing that the pathological findings of TCT can appear even before the symptoms, as has been mentioned, and can diagnose patients with initial false negatives by microbiology[26,27]. Therefore, it was concluded that TCT was a valuable tool capable of diagnosing COVID-19 infection (and its complications, such as thromboembolism) both in the initial ED assessment of pulmonary involvement and for follow-up, ideally always with microbiological confirmation when available[26,27]. Apart from TCT, lung ultrasound can also play a role in the evaluation of pneumonia and adult respiratory distress syndrome (ARDS) in COVID-19. As well as assessing the evolution at the patient's bedside. It has a higher sensitivity than CR in patients with moderate symptoms (75% vs. 59%). The most common findings that can be found are numerous B lines, pleural thickening and consolidation that can present bronchogram[26-28]. However, it is important to remember the need for personal protection precautions and equipment cleaning before and after use.

MICROBIOLOGICAL STUDIES:

The most important diagnostic tests for the detection of COVID-19 are molecular and serological[13]. The first provide information on the presence of replicating virus and the second on the defensive attitude of the host. Molecular diagnosis of COVID-19 is performed by detecting genomic sequences of SARS-CoV-2 in respiratory samples (in the case of nasopharyngeal or oropharyngeal swab in EDs, although they can also be determined in other biological samples). At the present time, when the pandemic is spreading globally, sensitive techniques (greater than 95%) are required, with which we can screen the population[13,29]. Quantitative reverse transcriptase polymerase reaction (rRT-qPCR) is the most frequently used. In recent months, TMA (transcription-mediated amplification) techniques have been used, which provide several advantages such as less instrumentation, less contamination in the laboratory because they operate on RNA that is more labile and a better detection capacity, greater than PCR and in less time (approximately 30 minutes per test), which, according to microbiology laboratories, is a highly recommendable method for EDs. Serologic diagnosis and its interpretation could be useful in certain situations in EDs. To review these situations, complementary information is referred to in recent documents of the GT-LATINFURG (Update of the Recommendations for action in cases of infection by the New Coronavirus SARS-CoV-2. Second Document August 2020)[13]. A permanent update of rapid tests approved by FDA or other regulatory societies and marketed in the United States or other countries of the world, with their sensitivity and specificity parameters, is available on the Johns Hopkins University website: https://www. centerforhealthsecurity.org/resources/COVID-19/serology/SerologybasedtestsforCOVID-19.html

Other microbiological screening tests:

- Blood cultures and other cultures directed according to focus if bacteremia or bacterial coinfection is suspected.
- In case of sepsis: antigenuria against Streptococcus pneumoniae and Legionella pneumophila.
- In case of epidemic period it is suggested to perform a rapid test for Influenza virus in respiratory secretions and even better, the availability of multitest for respiratory viruses (including SARS-CoV-2).

Other tests to be evaluated individually: electrocardiogram, urine sediment, etc.

ventional triage and in the isolation circuit, a more complete anamnesis should be performed, inquiring about the presence of symptoms of SARS-CoV-2 infection. If the suspicion of COVID-19 is confirmed, the patient should be evaluated in the isolation circuit and provided with a surgical mask and hand washing with hydroalcoholic solution. Otherwise, the patient should be taken to the conventional circuit[13,15,21].

Complementary tests available and recommended in the emergency department for patients with COVID-19

Currently, there is great variability in the availability of complementary tests (CT) in the ED between countries, as well as between centers within the same country according to region, type of hospital (public-private, level of complexity, etc.), despite the fact that all of them treat patients with severe infection (including COVID-19) and even have an intensive care unit (ICU)[12,13].

Once a case is suspected by clinical or epidemiological criteria, the diagnosis of COVID-19 must be confirmed. For this purpose, the following is used: clinical history and anamnesis and the CT to be performed in the emergency department (analytical, radiodiagnostic and microbiological) to obtain immediate or deferred results[7,13,14,22-29].

According to the authors, it is essential for the proper quality care of patients with suspected or confirmed COVID-19 that all EDs have availability (24 hours a day) of a battery of basic CTs that should be ensured by those responsible for the hospital centers, Health Systems or Ministries, as appropriate. Table 4 shows the complementary tests that the GT-LATINFURG recommends should be available in all EDs ("COVID-19 ana-

lytical profile", chest radiology (CR) and thoracic computed tomography (TCT) and microbiological diagnostic tests)[7,13,14,22-29].

Identification of the patient with COVID-19 in the emergency department: clinical criteria

The median incubation period is 56 days, with a range of 1 to 14 days. Of the symptomatic cases, 97.5% develop within 11.5 days of exposure. On the other hand, the median time from symptom onset to recovery is 2 weeks when the disease has been mild and 36 weeks when it has been severe or critical[7,13,16,30].

The detection of asymptomatic patients is complicated; in a seroprevalence study carried out in all regions of Spain during the first months of the pandemic, 33% of the cases were estimated to be asymptomatic[14,17]. After a few months, there is even talk of a higher proportion of asymptomatic than symptomatic cases among those detected (together with a clearly lower average age). This is an added problem, because they maintain the transmission capacity of COVID-19[31]. Some studies show that asymptomatic cases are more frequent in children. However, in both asymptomatic children and adults, a high proportion of radiological pulmonary alterations, such as multifocal opacities, has been observed in up to 70% of cases[26,27]. However, in general, in these cases inflammatory markers and cytokines are at the same level as in healthy individuals, indicating that these cases do not generate a detectable inflammatory response[7,13].

Individuals with SARS-CoV-2 generally develop relatively nonspecific signs and symptoms. In a study of 44,672 patients with COVID-19 in China, 81% had mild-moderate manifestations, 14% severe, and 5% critical (defined by respiratory failure, septic shock, and/or multiorgan dysfunction)[2,7].

In a series of 55,924 laboratory-confirmed cases at the beginning of the pandemic in China, the most common signs and symptoms were: fever (87.9%), dry cough (67.7%), fatigue (38.1%), presence of sputum (33.4%), shortness of breath (18.6%), odynophagia (13.9%), headache (13.6%), myalgias and/or arthralgias (14.8%), chills (11.4%), nausea or vomiting (5.0%), nasal congestion (4.8%), diarrhea (3.7%), hemoptysis (0.9%) and conjunctival congestion (0.8%)[2]. Other SRs and meta-analyses, such as those published by Fu et al.[32] and Yang et al.[33] (Table 5) showed a similar spectrum of symptoms, where fever was the most frequent symptom. However, the presence of fever is not an unequivocal finding, as fever may be absent or maintain a temperature below 38°C. On the other hand, pneumonia seems to be the most frequent severe manifestation in COVID-19 patients, characterized mainly by fever, cough, dyspnea and bilateral infiltrates on chest imaging[33] (Table 5).

At the beginning of the pandemic, COVID-19 was preferentially associated with respiratory viral infection symptoms (fever, dyspnea, throat discomfort, cough, sputum, rhinorrhea, nasal congestion and conjunctivitis, among other symptoms)[2,7]. As the first weeks passed, it was confirmed that some patients experience other symptoms such as anosmia, ageusia, nausea, vomiting, diarrhea, abdominal pain, and mainly a variety of neurological and dermatological symptoms[7,32,33]. For a more complete review of the full spectrum of presenting signs and symptoms of COVID-19, reference is made to the supplementary information in recent GT-LATINFURG documents described in the method section of this CD[13].

Table 5. Clinical manifestations of COVID-19

Symptoms	Number of studies	Number of patients	Prevalence: % (95% CI)
Fever	36	2,817	83.3 (78.4-87.7)
Cough	36	2,792	60.3 (54.2-66.3)
Fatigue	23	2,116	38.0 (29.8-46.5)
Myalgia	21	2,094	28.5 (21.2-36.2)
Increased sputum	16	2,042	26.9 (18.3-36.4)
Dyspnea	13	1,981	24.9 (16.6-34.4)
Chills	4	1,222	15.0 (0.3-41.4)
Chest pain	9	423	14.9 (4.9-28.4)
Headache	20	2,312	10.4 (9.9-18.6)
Odynophagia	18	2086	12.3 (8.5-16.5)
Dizziness	4	270	7.6 (0.0-23.5)
Diarrhea	25	2,415	8.4 (4.8-12.6)
Rhinorrhea	6	290	3.5 (0.8-7.4)
Nausea/vomiting	7	1,452	3.6 (1.0-7.4)
Hemoptysis	3	1,202	2.0 (0.0-11.4)
Nasal congestion	5	1,248	1.8 (0.4-3.9)
No clear sym-ptoms	11	542	5.6 (1.4-11.6)

95% CI: 95% confidence interval.
Adapted from references 13 and 32.

An SR has recently been published by the Cochrane Library by Struyf et al.[34] which aims to answer the questions: what is the diagnostic validity of symptomatology for suspected COVID-19? can symptoms and medical examination accurately diagnose COVID-19 disease in the ED? This review used 16 studies and 7,706 patients. The prevalence of COVID-19 ranged from 5% to 38% (median 17%). Four of these studies were conducted in the ED (1,401 cases). Twenty-seven independent symptoms and signs were reviewed and grouped into 4 categories: systemic, respiratory, gastrointestinal, and cardiovascular. Most had low sensitivity and high specificity. Only 6 had a sensitivity greater than 50%: cough, sore throat, fever, myalgias or arthralgias, fatigue and headache. The presence of fever, myalgias/arthralgias, fatigue and headache would have a likelihood ratio of at least 5 and a specificity greater than 90% (Table 6). This could mean (when there is no

Table 6. Individual diagnostic performance results of some of the most frequent COVID-19 symptoms

Symptoms	Sensitivity rate	Specificity rate
Cough	43%-71%	14%-54%
Sore throat	5%-71%	55%-80%
Fever	7%-91%	16%-94%
Myalgia and/or arthralgia	19%-86%	45%-91%
Fatigue	10%-57%	60%-94%
Headache	3%-71%	78%-98%

Adapted from references 13 and 34.

Table 7. Hematological parameter findings in patients with suspected or confirmed COVID-19

Parameter	Clinical significance	Frequency of occurrence
Lymphopenia	Suspected COVID-19 in epidemiological context. Association with increased severity of COVID-19.	60-83%
Leukopenia	Association with increased severity of COVID-19.	29-40%
Leukocytosis	Bacterial superinfection.	1-10%
Neutrophilia	Bacterial superinfection. Suspected hyperinflammatory syndrome and cytokine storm.	1-10%
Thrombopenia	Consumption coagulopathy (sepsis or disseminated vascular coagulation).	31-58%
Elevated D-dimer	Association with increased severity of COVID-19. Suspected thromboembolic disease in clinical and epidemiological settings.	40-60%
Elevated prothrombin time	Association with increased severity of COVID-19. Consumption coagulopathy.	40-60% (Aprox)
Elevated FDP	Association with increased severity of COVID-19. Consumption coagulopathy.	40-60% (Aprox)
Elevated ferritin	Association with greater severity of COVID-19. Suspected macrophagocytic-like syndrome.	40-60%

Adapted from references 13 and 38.
FDP: fibrinogen degradation products.

suspicion of involvement of other viruses) that the existence of these symptoms would increase the probability of diagnosis of COVID-19, especially in situations of community transmission[34]. The individual signs and symptoms included in this SR seem to have a very limited diagnostic capacity. Therefore, according to currently available data, neither the absence nor the presence of these individual signs or symptoms is sufficiently accurate to rule out or confirm COVID-19. Although we already know the profile of the patient with COVID-19 who attends the ED[35,36] studies are needed with a combination of several of these symptoms and signs in order to find a predictive model with greater capacity to make the appropriate diagnostic and therapeutic decisions in the ED (perform confirmatory microbiological tests, decide on admission or discharge, decide on appropriate treatment, etc.)[34].

Identification of the patient with COVID-19 in the emergency department: analytical criteria

In a recent meta-analysis, Li et al.[22] reported that clinically symptomatic patients with COVID-19 presented the following as the most frequent laboratory alterations, which would suggest an unconfirmed diagnosis of COVID-19 in compatible clinical and epidemiological situations: lymphopenia (64.5%), increased C-reactive protein (CRP) (44.3%), increased lactate dehydrogenase (LDH) (28.3%) and leukopenia (29.4%).

COVID-19 has been associated with a state of hypercoagulability related to inflammatory changes different from the classic disseminated intravascular coagulation characteristic of other serious pathologies such as sepsis. Although a frequent elevation of fibrinogen or D-dimer has been detected, the pathogenesis of this hypercoagulable condition remains to be determined, but COVID-19 is also associated with an increase in ferritin and prothrombin time and thrombopenia, as an expression of disease severity and consumption coagulopathy[37,38].

Alterations in blood cell counts such as lymphopenia and leukopenia (together with the aforementioned thrombopenia) are also frequent in critically ill patients (especially lymphopenia in critically ill patients) (Table 7). Lymphopenia represents a defective immune response of the patient against SARS-CoV-2 and is present in one third of adult patients (only 3% of children) and increases in those with severe symptomatology (up to 6483% of cases)[39]. A SR and meta-analysis evaluating 24 studies with 3,099 patients shows that the existence of lymphopenia when the patient arrives at the hospital is associated with worse evolution in patients with COVID-19. It establishes an odds ratio (OR) of 3.70 (95% CI: 2.44 to 5.63) for the relationship between lymphopenia and severely critical COVID-19[39].

Leukocytosis, if present, suggests bacterial coinfection or superinfection[38].

One can also appreciate how neutrophilia can appear in the context of cytokine storm and hyperinflammatory state[38].

Both increased triglycerides and ferritin are associated with SARS-CoV-2-associated hemophagocytic-like syndrome[38].

Finally, thrombopenia is present from 31% of mild-moderate patients to 58% in patients with severe COVID-19, which translates into an OR of 2.96 (95% CI: 2.07-4.22) in relation to its association with severity[39].

On the other hand, hepatic cytolysis has been found in up to 1/3 of patients with COVID-19[7,13,14,22]. Along these lines, the presence of hepatic alterations has been reported, especially in the most severe or critical patients, as an expression of hepatic insufficiency reflected by an increase in transaminases, bilirubin and prolongation of prothrombin time[37,38].

Also, elevation of LDH has been observed in up to 76% of the most severe patients and, to a lesser extent, of creatinine phosphokinase (CPK)[37,38].

The increase in CRP (together with the increase in D-dimer and ferritin) seems to represent the existence of greater inflammation, worse prognosis and mortality. CRP is elevated in 75-93% of patients with COVID-19 and with greater intensity and frequency in severe patients[37,38].

Table 8. Findings of biochemical parameters in patients with suspected or confirmed COVID-19

Parameter	Clinical significance	Frequency of occurrence
Elevated C-reactive protein (CRP)	Suspected COVID-19 in epidemiological context. Association with greater severity of COVID-19. Association with higher SARS-CoV-2 viral load.	75%-93%
Elevated procalcitonin (PCT)	Bacterial superinfection. Association with increased severity of COVID-19.	Greater in intensive care
Elevated lactate dehydrogenase (LDH)	Suspected COVID-19 in epidemiological context. Associa-tion with increased severity of COVID-19. Association with lung damage and multiorgan damage.	28-41%
Elevated bilirubin	Association with increased severity of COVID-19. Association with liver involvement. Association with antiretroviral treatment.	Variable according to clinical involvement
Elevation of alanine aminotransferase (ATL) and aspartate aminotransferase (ATS)	Association with greater severity of COVID-19. Association with liver involvement. Association with antiretroviral treatment.	Variable according to clinical involvement
Elevation of serum creatinine	Association with increased severity of COVID-19. Association with renal involvement.	15-60%
Elevated troponin	Association with increased severity of COVID-19. Association with cardiac involvement.	Variable according to clinical involvement
Creatinine phosphokinase (CPK) elevation	Association with increased severity of COVID-19. Association with cardiac involvement. Association with rhabdomyolysis (especially in young people).	Variable according to clinical involvement
Decreased albumin	Deterioration of liver function.	10-25%
Elevation of blood glucose	Some patients develop ketoacidosis (these disorders may also be associated with antiretroviral therapy).	1-10%

Adapted from references 13 and 38.

The "cytokine storm" is reflected in the increase in IL-1B, IL-6, IL-7, IL-8. The combined determination of IL6 and D-dimer allows us to relate the combined elevation of the 2 determinations with a greater efficacy in the prognosis of the severity of COVID-19. Thus, IL-6 values above 24.3 pg/mL (related to the cytokine storm) are considered to be higher[38-40]. Therefore, although the result of IL-6 determination cannot be known immediately in most EDs, it is useful to obtain it in the ED to assess the degree of inflammatory response on arrival at the ED and for making therapeutic decisions[12,13].

On the other hand, the increase in procalcitonin (PCT) may play an important role in predicting a worse course of the disease. Its increase, with or without an increase in the leukocyte count, indicates the existence of bacterial coinfection[40] (Table 8).

Identification of the patient with COVID-19 in the emergency department: radiological criteria

The most important finding within this entity is SARS-CoV-2 pneumonia.

CR typically shows bilateral alveolar infiltrates in a high percentage. However, this may be normal in early infection (first days) and show an evident radiological progression after the seventh day. Thus, up to 50-60% of patients may have more or less subtle, focal or scattered, localized or extensive, unilateral or bilateral changes, compatible with the diagnosis of COVID-19[26,27].

While there are no pathognomonic radiological patterns of COVID-19, radiological patterns or lesions compatible and suggestive of COVID-19 on CR (Figure 3), especially in the compatible epidemiological context, are[26-28]:

– Existence of focal opacities (with a clear increase in radiologic density with partially defined margins, although less than a nodule) or, occasionally, faint focal opacities (less defined than the previous ones).
– Unilobar or multilobar patchy consolidations.
– Focal or diffuse interstitial pattern (linear images, with peribronchial enhancement).
– Focal or diffuse alveolointerstitial pattern.
– Pattern in dazzled video.
– Combinations of the previous ones.

On the other hand, there are a number of lesions NOT suggestive of this disease[26-28]: 1) single focal consolidation, with or without air bronchogram or silhouette sign, 2) lymphadenopathy, 3) pleural effusion, 4) nodules.

One of the characteristics associated with severe disease and the onset of adult respiratory distress syndrome (ARDS), which requires intensive therapy, is rapid radiological progression (together with clinical worsening) within hours or days.

The lower sensitivity of CR for the detection of video-blurred opacities, the most frequent finding in COVID-19 pulmonary infection that can go undetected, has been postulated as the reason for the low sensitivity of CR compared to TCT (less than 60% vs. 95-98%, respectively) in the initial diagnosis of this infection[26-28].

Regarding TCT, it has greater sensitivity and specificity than CR, so if it is available and there is no contraindication (for example: clinical situation, allergy to contrasts, pregnancy, etc.), it would be the ideal test to perform in the ED. In addition to having a greater capacity to diagnose pulmonary alterations (up to 80-90% of symptomatic cases and up to 60-70% of asymptomatic cases), it is able to better define the extent of the lesions, location, possible complications (for

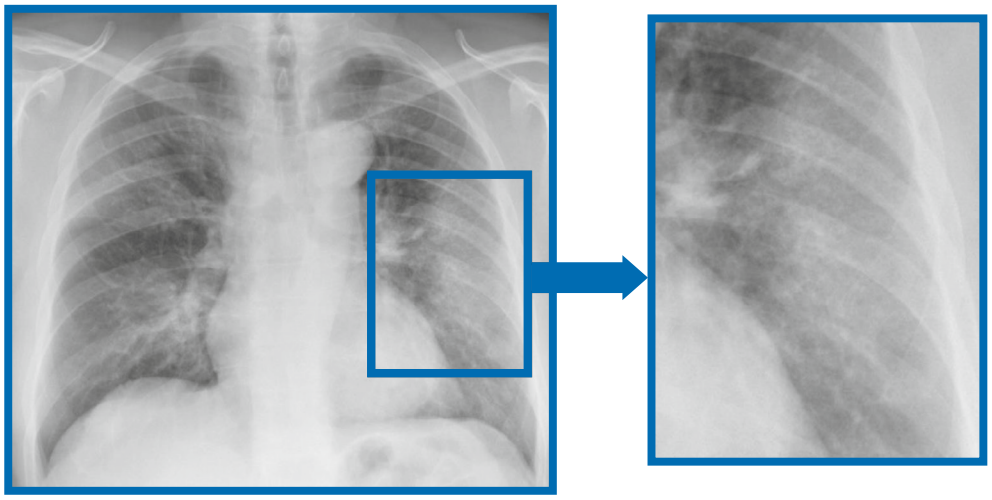

Figure 3. SARS-CoV-2 pneumonia. Diffuse interstitial thickening with faint peripheral ground-glass density infiltrate bilaterally, more visible in left hemithorax (detail). Pattern compatible with COVID-19. Image courtesy of the Radiodiagnostic Service of the Complejo Hospitalario Universitario de Toledo, Spain.

example: pneumothorax, effusion, pulmonary thromboembolism, etc.). On the other hand, the patient must be moved and the test takes longer to perform. Lung lesions have been found to be detected in TCT studies from even before the onset of symptoms up to day 14 after the onset of symptoms, with a mean of 4 days[26,27,41].

TCT achieves a sensitivity of 86-97% for detecting findings suspicious for COVID-19. Even the higher the clinical severity, the higher the sensitivity. Similarly, TCT has proven to be capable of detecting alterations compatible with COVID-19 even before symptoms appear or the detection of SARS-CoV-2 by detection of positive PCR, in patients with inconclusive plain chest X-ray. The median time of appearance of lesions on TCT is 4 days from the onset of symptoms (with an interval from before symptoms appear to 14 days later). Although, a TCT with normal features cannot exclude the diagnosis of COVID-19[26,27,41].

On the other hand, lesions observed in TCT can be changing and "dynamic". It seems that they can evolve, hence they have been called "migratory lesions", in which there is absorption of the primary lesions and the emergence of new lesions[26,41]. Some studies showing the existence of pneumonia show that up to 75% of them were bilateral pneumonias[26,27,41].

Radiological patterns or lesions compatible and suggestive of COVID-19 on TCT, especially in the compatible epidemiological context, are[26,27,41]:

– Tarnished or ground glass opacities (the most frequent). This is described as pulmonary parenchymal opacification that produces a minor increase in attenuation compared to consolidation, so that despite the increase in density, the pulmonary vessels and bronchial walls of the affected parenchyma are still differentiated. They represent a partial occupation of the airspace, are less opaque than consolidations and, therefore, TCT is more sensitive in their detection than CR.
– Single patchy consolidations, although they are more often multiple. Referring to the occupation of the airspace by pathological products (pus, water, blood, etc.). Consolidation appears as a homogeneous increase in pulmonary parenchymal attenuation (increased density) that obscures the vessel margins and airway walls. The air bronchogram sign, which refers to the visualization of air-filled bronchial lumina within a pulmonary parenchymal opacity and thus implies airway patency, may be present.
– Interstitial changes of peripheral and basal distribution (nodular, interstitial and interlobular septal thickening).
– Bronchiectasis.
– Crazypaving pattern. It is characterized by a thickening of the inter- and intralobular septa. This is superimposed on the ground-glass opacities, simulating a cobblestone floor, a finding that is also much more easily identified in TCT than in CR.

TCT involvement is related to the evolution and prognosis of the patient. Recently, Ruch et al.[41] suggested an algorithm based on the extent of pulmonary involvement in TCT with the ability to predict patient mortality and, therefore, the need for admission to the ICU. Consequently, upon suspicion of COVID-19 in the ED, TCT should be performed and, depending on the pathological findings (assessing the proportion of lung fields affected), it would be associated with a worse outcome (understood as admission to the ICU or death within 7 days): 1) if the involvement is ≤ 25% in 22.9% of cases, 2) if the involvement is 26-50% in 40.9% and, 3) if it is > 50% in 69.5% of cases.

In addition to CR and TCT, as the most commonly used radiodiagnostic tests, clinical lung ultrasound (CLUS) could be of diagnostic help in patients with suspected non-critical respiratory infection by SARS-CoV-2 where CR does not show obvious findings[42]. A study has recently been published where the most frequent

findings in cases of confirmed COVID-19 were focal and confluent B-lines with associated pleural irregularities in posterobasal lung areas. The diagnosis of COVID-19 by CLUS was estimated to have a sensitivity of 92.6% (95% CI: 75.7-99.1), specificity of 85.2% (95% CI: 66.3-95.8), positive predictive value of 75.8% (95% CI: 59.6-91.9) and negative predictive value of 92% (95% CI: 73.9-99.1)[42].

Identification of the patient with COVID-19 in the emergency department: microbiological criteria

SARS-CoV-2 virus can be detected initially 12 days before the onset of symptoms in upper respiratory tract specimens, as well as in asymptomatic individuals. On the other hand, the virus can persist for 7 to 12 days in moderate cases and up to 46 weeks in severe cases[2]. The first cases considered to be reinfection by SARS-CoV-2 (different strains confirmed)[43] have recently been documented.

Positivity in molecular techniques indicates the presence of the virus in the respiratory tract, thus confirming that the person has been infected. However, this result does not necessarily indicate active infection and risk of virus transmission[2,44]. The criteria for ruling out active infection are: 1) clinical, if more than 10 days have passed since the onset of symptoms and 3 additional days without symptoms, or 10 days since the molecular test was positive in asymptomatic persons; 2) microbiological, presence of positive IgG with negative IgM for SARS-CoV-2. The molecular test can remain positive for 3 to 4 weeks, even for months if ultra-sensitive TMA tests are performed, and particularly in persons with more severe infection[45] (Table 4). Occasionally the presence of RNA in nasopharyngeal exudates is intermittent. For these reasons, once a positive result has been obtained by molecular technique it is not indicated to repeat it, except in the case of healthcare workers in whom a negative molecular technique is required to return to work[31,44].

Criteria for requesting a microbiological sample and approach:

- Scenario 1: there are occasional cases, but most of them are related to origin from risk areas or contact with confirmed cases or cases under investigation. Cases in microbiological investigation of COVID-19 will be considered to be those that meet the criteria defined by the different Ministries of Health. The definitions and concepts, as well as the changes they have undergone in Latin America and Spain, can be consulted and compared in previous publications of the GT-LATINFURG[13].
- Scenario 2: there is sustained and increasing community transmission. Cases under microbiological investigation for COVID-19 will be considered those that meet clinical criteria, independently of epidemiological criteria and with the aim of not increasing nosocomial transmission, which is estimated at 41%[13,31]. In this scenario, testing will only be prioritized in patients who are going to be admitted for pneumonia or comorbidity destabilization due to viral infection. Patients with minor symptoms at home, in Primary Care Centers and in the ED will be referred home with symptomatic treatment, with the test being performed as soon as possible, in a deferred manner from there through Public Health personnel. Healthcare workers with minor symptoms would be given priority in the performance of the test as soon as possible in order to return to work.

Currently, the availability of the rapid antigen detection test against SARS-CoV-2 (by means of immunochromatography -lateral flow- and obtaining the sample with a swab from the nose or throat) is presented to the ED as a new useful tool for the diagnosis of COVID-19, since: 1) the results are obtained in 15-20 minutes in the ED itself (no specific instrumentation is needed) with the help it provides for ED decision-making; 2) the cost is lower than that of other tests and its availability will only depend on the existence of specific kits; 3) the approved ones in Spain, for example, have shown a sensitivity of 93% and a specificity of 99%. When the test is positive in a suspected patient, it will be definitive and the patient will have to be isolated in the ED until discharge or admission is decided. If the test is negative, in the case of high suspicion and clinical involvement, RT-PCR should be considered. The target patient for this test would be, at present, those who come to the ED in the first 57 days from the onset of symptoms (in which there would be a high viral load)[46]. The implementation of the "point of care" is recommended in EDs where, in addition to the detection of SARS-CoV-2 antigen, seasonal respiratory viruses can be performed.

Risk factors, admission, severity and mortality of patients with COVID-19

Most people infected with SARS-CoV-2 virus have a mild illness with subsequent recovery and a significant proportion (variable in each country) even have oligosymptomatic COVID-19[7]. However, even in these patients, certain clinical signs can be observed, such as febrile fever in the days prior to diagnosis and even alterations in TCT, including ground-glass opacities or patchy swelling[26]. As has also been mentioned, 80% of confirmed patients develop mild to moderate disease, which also includes cases of pneumonia. Severe disease (dyspnea, respiratory rate $\geq$ 30/minute, blood oxygen saturation $\leq$ 93%, PaO_2/FiO_2 ratio < 300, and pulmonary infiltrates > 50% of the lung field in 24-48 hours) accounts for 14%, and, finally, 6% may present as critical disease (severe respiratory failure, septic shock and/or multiorgan dysfunction)[2,7]. However, Richardson et al.[47] in their study found that up to 12.2% of these patients required invasive mechanical ventilation. The severity of patients with COVID-19 varies according to geographical location and other factors. In this regard, age appears to be the first risk factor for developing

Tabla 9. Risk factors associated with severe COVID-19

Age over 65 years old*.
Male sex.
Chronic respiratory system disease (e.g., chronic obstructive and asthma).
High blood pressure.
Diabetes mellitus.
Cardiovascular disease (heart failure, coronary artery disease, arrhythmias).
Obesity (BMI ≥ 30).
Chronic kidney disease.
Chronic liver disease.
Neoplastic pathology.
Immunosuppression (including transplantation, HIV infection with CD4 < 200 cels/mcl, biological therapy or other immunosuppression)**.

*Age has been associated with greater severity and mortality; however, a cut-off point has not been clearly established. An age of 65 years is established as the cut-off point in several studies.
**The US CDC (Center for Disease Control and Prevention) considers immunosuppression as a risk factor for other respiratory pathogens, although its role as a risk factor for COVID-19 is unknown and requires further evidence. Adapted from references[7,13,48-51].
BMI: body mass index; HIV: human immunodeficiency virus.

COVID-19 and influences prognosis[2,7,13]. Older patients are not only those most affected by COVID-19, but also those with the worst prognosis[7]. In contrast, symptomatic infection in children is not only infrequent, but if symptomatic, it is milder in nature. However, severe cases have been described in which a multisystemic inflammatory syndrome with a worse prognosis stands out[48].

Other risk factors described in patients with COVID-19 are shown in Table 9. The male sex is associated with a higher proportion of deaths compared to the female sex. However, the most severe clinical outcome occurs in those patients who also have some comorbidities[7,13]. In the SR-meta-analysis by Yang et al.[33], the most frequent comorbidities were hypertension with 21.1% of cases (95% CI: 13.0% to 27.2%) and diabetes 9.7% (95% CI: 7.2% to 12.2%), followed by cardiovascular disease 8.4% (95% CI: 3.8% to 13.8%) and chronic respiratory disease with 1.5% (95% CI: 0.9% to 2.1%). The cardiovascular disease associated with the worst prognosis was heart failure. In addition to the comorbidities described, other studies include obesity, chronic renal failure, chronic obstructive pulmonary disease (COPD) and neoplastic pathology[7,47,49-52]. Immunosuppression (including HIV infection and the use of biologic therapy) is considered as a risk factor for other respiratory pathogens, although its role as a risk factor for COVID-19 is unknown and requires further evidence[7,47].

On the other hand, some laboratory data have been associated with severe COVID-19 disease. Although their prognostic value has not been clearly demonstrated, Table 10 considers findings to be taken into account to identify those patients who could be at risk of greater severity. These include lymphopenia and increased D-dimer[37-40].

Patients with some or all of the risk factors shown in Tables 9 and 10 had higher mortality than that reported overall among patients treated in the ED (between 11.9% and 21% depending on the study)[35,47,53].

Table 10. Laboratory data related to COVID-19 severe*

Lymphocytes < 800 cells/microliter.
D-dimer > 1,000 ng/ml.
CRP > 10 mg/dl (> 100 mg/l).
LDH > 245 UI/L.
Troponin 2 times or more above the upper limit of normal.
Ferritin > 500 mcg/l.
CPK 2 times or more above the upper limit of normal.
IL-6 > 24.3 pg/mL.
PCT > 0.5 ng/mL (indicates bacterial superinfection).

*These findings are considered to be taken into account to identify those patients who could be at risk of greater severity (they should be adapted to the normal laboratory values of each center). Adapted from references 13, 37-40.
CRP: C-reactive protein; LDH: lactate dehydrogenase; CPK: creatinine phosphokinase; IL-6: interleukin-6; PCT: procalcitonin.

Finally, about 3.5% of patients discharged from hospital after hospitalization return to the ED within 14 days. The most frequent cause is respiratory distress and difficulty and the associated factors are COPD and arterial hypertension[54].

Biomarkers of inflammation and infection as an aid in the diagnosis and prognostic assessment of patients with COVID-19

Clinical manifestations of infectious processes (bacterial and viral such as COVID-19) are often nonspecific and variable (especially in elderly or immunocompromised patients), which makes early recognition of these patients and these situations difficult. Infection and inflammatory response biomarkers (IIRBM) have become tools of great help to the clinician in improving diagnosis (and therefore the correct treatment of bacterial or viral infection), and risk stratification and prognosis (and thus facilitating and advancing urgent decision making)[23].

Currently, most countries of the GT-LATINFURG members and the rest of Latin America have centers with IIRMB. However, this is the CT with the greatest differences in terms of its availability for EDs[12]. Lactate is available in 100% of EDs in Spain with an ED laboratory, but other countries only have 40-80% availability, and in some of them it is not available 24 hours a day (although it is available for other services such as the ICU). Similarly, CRP (a marker of severity in COVID-19) is not available in a considerable number of EDs[12,13].

PCT is already available and used in more than 75% of EDs in Spain, with similar or higher figures in the USA and 5-25% in many centers in other countries. Although it could be available in all countries, actual use in the ED today is very diverse: there is a high level of PCT use in Mexico and Ecuador, a "medium level" in Colombia, Chile and Argentina and a limited level in Costa Rica, Panama, Dominican Republic, Uruguay and Peru. In the rest of the Latin American countries, PCT is used only occasionally or not at all in the ED[12].

Other IIRMB such as proadrenomedullin (proADM), soluble urokinase-type plasminogen activator receptor (suPAR), presepsin (soluble receptor subtype CD14), interleukins (IL-6, IL-8), tumor necrosis factor (TNF), or the surface receptor expressed on myeloid cells (sTREM1), etc., can be requested in less than 1% of EDs in our countries today, but are expected to be useful tools in the future[12].

In this regard, in the initial clinical assessment of the COVID-19 patient with suspected bacterial coinfection, the determination of PCT is recommended to confirm the clinical suspicion, the possibility of bacteremia, and to guide the initiation and interruption of antibiotherapy together with specific treatment for SARS-Cov-2[23,40,55]. On the other hand, to quantify severity and stratify risk, identifying patients with severe infection and at risk of poor outcome or death. Although PCT has been used for this purpose in the patient with pneumonia[23], initial assessment of lactate and of proADM is recommended if available. ProADM or suPAR, which have been positioned for the near future as the IIRMB with the potential availability and best prognostic capacity for mortality in patients with sepsis, pneumonia and also with COVID-19 (or in combinations of the 3 previous situations)[56-58]. Thus, high concentrations of proADM[57] and/or suPAR[59,60] are associated with greater severity, risk and admission rates, respiratory failure and the need to transfer the patient to intensive care, and with greater mortality, which would help us to decide on admission, intensify antiviral and anti-inflammatory therapy.

To quantify severity and stratify risk, identifying patients with severe infection and at risk of poor outcome or death, PCT has been used for this purpose in patients with pneumonia[23]. However, initial assessment of lactate and proADM or suPAR, if available, is recommended. Both have been positioned for the near future as the IIRMB with the potential availability and better prognostic capacity for mortality in patients with sepsis, pneumonia and COVID-19 (or combined)[56-58].

In fact, the combined use of diagnostic and severity biomarkers (PCT and lactate in the lead) is nowadays recommended, as they enhance each other and increase specificity and prognostic performance ("biomarker synergy"). Especially those that maintain their diagnostic (PCT) and prognostic capacity (lactate, proADM and suPAR) in the subgroups of patients who, precisely, have less expressive clinical manifestations and are more vulnerable (elderly, immunocompromised, renal, diabetic, etc.)[55-57].

In the opinion of the authors, the usefulness of the IIRMB as a tool to assist in the diagnosis, prognosis and adequacy of antibiotic treatment and support is unquestionable. Therefore, together with the initial analysis, the universal availability and assessment of lactate, CRP and PCT is currently recommended, and in the future the availability of ADM and/or suPAR would be included in the portfolio of services[23,55-60].

Discussion and conclusions

Having reviewed the 10 key points on COVID-19 in the ED considered by the authors (Table 1), we have identified some of the relevant obstacles and problems for carrying out such care. Table 11 shows some proposals, strategies or recommendations to be adopted by hospitals, health systems or competent administrations that we believe are applicable to any environment and reality in our countries. Always depending on the local characteristics and existing possibilities, but in all cases with the same objective: to try to overcome the existing barriers and problems in order to improve the care of our patients suffering from COVID-19 as much as possible.

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Table 11. Description of some existing problems and obstacles to the proper care of patients with COVID-19 in the ED and proposals for their improvement or resolution

Problems and obstacles	Improvement proposals and strategies
Lack of sufficient anticipation and specific contingency plans for EDs in the care of patients with COVID-19 in the face of the enormous impact of the pan-demic in GT-LATINFURG member countries and the arrival of the flu season.	Development of expansion and contingency plans in all EDs and centers to avoid repeating the lack of space, personnel and material suffered in the first wave of the pandemic.
Lack of healthcare personnel, personal protective equipment (PPE, masks, gowns, goggles, etc.), SARS-CoV-2 diagnostic tests, and healthcare facilities.	Guarantee the existence of space, personnel and material necessary to ensure both the assistance to patients with COVID-19 in the ED and the safety and protection of healthcare personnel, avoiding infections and casualties among them.
Failure to assess and record vital signs: blood pressure, heart rate, respiratory rate, temperature and level of consciousness. Oxygen saturation by pulse oxime-try.	Implement local/national guidelines that include the registration (Check-list) of vital signs and oxygen saturation by pulse oximetry for the correct clinical as-sessment.
Variability in the use of diagnostic criteria and definitions of confirmed cases, suspects, contacts, etc. between countries.	Implement international guidelines that include the definitions and concepts to be used by all centers in order to reach a consensus on procedures and be able to establish real and adequate comparisons.
Lack of double care circuit in the ED and establishment of triage before admis-sion to the ED.	Dual set-up: triage, entry, circuits, equipment, personnel, resources and materials for COVID-19 patients and others.
Lack of a structured triage system and/or computerized alarm system. – Saturation and high pressure in the ED in most centers and countries.	Implement a triage system so that the prioritization of patients with COVID-19 is effective in the face of the great pressure of care and saturation of the ED.
Variability and unspecificity of clinical symptomatology (especially in the elder-ly, neutropenic, diabetic, immunosuppressed and patients with renal, hepatic, onco-haematological comorbidity, etc.).	Ensure the availability in the ED of objective diagnostic aids ("COVID-19 pro-file", radiology and computed tomography, microbiological tests for SARS-CoV-2). Implement ultra-fast Point-of-Care tests.
Lack of availability of diagnostic and assessment tests in the ED, sometimes only available in the ICU, such as biomarkers.	Define in each center and country the basic complementary tests that should be available in all EDs and implement them. As well as tests that can optimize the care of patients with COVID-19 in the ED.
Lack of local regulations/diagnostic protocols (in each center) adapted to the different realities based on National or International Guidelines to establish the management and antiviral, anti-inflammatory, supportive treatment, etc.	Develop and implement local/national guidelines adapted to each center that list the therapeutic measures and their order to be carried out in the ED.
Underdiagnosis in the ED and delayed detection of the patient with COVID-19 are the first barriers to isolation, early and appropriate administration of time-ly treatment and admission decision.	Improve diagnosis and early prognostic assessment in the ED from triage (with/without electronic alerts) with the immediate request for laboratory tests, biomarkers, blood cultures, microbiological tests to confirm SARS-CoV-2, etc., to allow the decision of admission/discharge, and the administration of appro-priate and early treatment.
Lack of and limited ED treatment line items for COVID-19 (although available in the ICU and other hospital services).	Existence of a stock of medications in the ED itself (agreed upon with the hos-pital's infection committee and management) to guarantee coverage for all pa-tients, especially those who are discharged.
Lack of epidemiological and clinical data registries related to COVID-19 for its evaluation and usefulness as a tool for improving SARS-CoV-2 patient care.	Promote basic epidemiological and clinical studies and research to learn about patient characteristics and local points of improvement.
Lack of training and multiprofessional teams (medicine and nursing) for the diagnosis and treatment of COVID-19. Often high turnover of professionals in the ED.	Design a local/national mandatory training plan for all ED staff involved in the care of these patients.
Lack of multidisciplinary teams for the care of SARS-CoV-2 patients.	Implementation of multidisciplinary units "COVID-19 Code".
Contamination of fomites (computer keyboards, paper medical records, surfac-es, materials, etc.) in the ED which can act as passive vectors transmitting COVID-19.	Systematic disinfection of the entire ED with separate cleaning of both circuits (COVID-19 and "the clean one"). Elimination of paper in medical records, non-essential material and disinfection of utensils after use.

ED: hospital emergency department; ICU: intensive care unit.

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