The Daily COVID-19 Literature Surveillance Summary

January 07, 2021

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".

Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

** OCEBM Table of Evidence Working Group = Jeremy Howick, Iain Chalmers (James Lind Library), Paul Glasziou, Trish Greenhalgh, Carl Heneghan, Alessandro Liberati, Ivan Moschetti, Bob Phillips, Hazel Thornton, Olive Goddard and Mary Hodgkinson*

EXECUTIVE SUMMARY

Adjusting Practice During COVID-19

- A team of cardiologists and pharmacists from hospitals in Shanghai and Wuhan, China assessed the association between mortality in hospitalized COVID-19 patients (n=535) and low molecular weight heparin (LMWH) use between January 26-March 26, 2020. They found overall adjusted odds ratio for mortality was lower in the LMWH-users vs non-users (0.20; 95% CI, 0.09-0.46), specifically in severe (0.08; 95% CI, 0.01–0.62) and critically ill cases (0.32; 95% CI ,0.10–0.996). Authors suggest LMWH appears correlated with a survival benefit in hospitalized COVID-19 patients, especially those severely and critically ill.

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ESTIMATING THE HERD IMMUNITY THRESHOLD BY ACCOUNTING FOR THE HIDDEN ASYMPTOMATICS USING A COVID-19 SPECIFIC MODEL

Kaushal S, Rajput AS, Bhattacharya S, Vidyasagar M, Kumar A, Prakash MK, Ansumali S.. PLoS One. 2020 Dec 16;15(12):e0242132. doi: 10.1371/journal.pone.0242132. eCollection 2020.
Level of Evidence: 5 - Modeling

BLUF

An interdisciplinary group of researchers from India present a mathematical model to approximate the threshold for developing herd immunity to COVID-19. Their model assumes that asymptomatic infections, which are estimated to account for ~50% of total infections, contribute substantially to herd immunity. This assumption allows their model to estimate the threshold for herd immunity to be 10-25% (Figure 1), which is much lower than previous predictions of ~70%. While this study provides a more optimistic estimate, it has substantial limitations including a heavy reliance on hypothetical modeling of COVID-19 transmission dynamics (Figure 2) and use of data obtained during the first wave of the pandemic.

ABSTRACT

A quantitative COVID-19 model that incorporates hidden asymptomatic patients is developed, and an analytic solution in parametric form is given. The model incorporates the impact of lock-down and resulting spatial migration of population due to announcement of lock-down. A method is presented for estimating the model parameters from real-world data, and it is shown that the various phases in the observed epidemiological data are captured well. It is shown that increase of infections slows down and herd immunity is achieved when active symptomatic patients are 10-25% of the population for the four countries we studied. Finally, a method for estimating the number of asymptomatic patients, who have been the key hidden link in the spread of the infections, is presented.

FIGURES

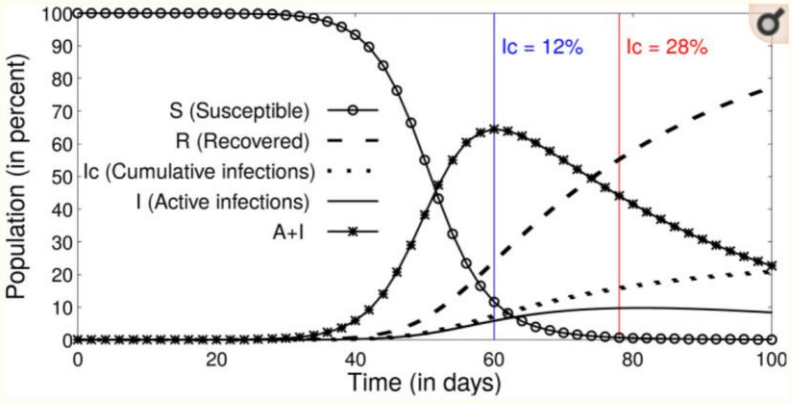

Fig 11

Analytical solution of the SAIR model with no lock-down using parameters for France ($\alpha_0 = 0.28$, $\gamma = 0.02$, $\delta = 0.01$.

The blue and the red lines indicate the maxima, considering only the symptomatic or the total infections respectively. The infection rate slows down significantly and a herd-immunity is achieved after the combined infections reach a peak when the symptomatic infections have crossed ≈ 12% of the total population.

Figure 1.

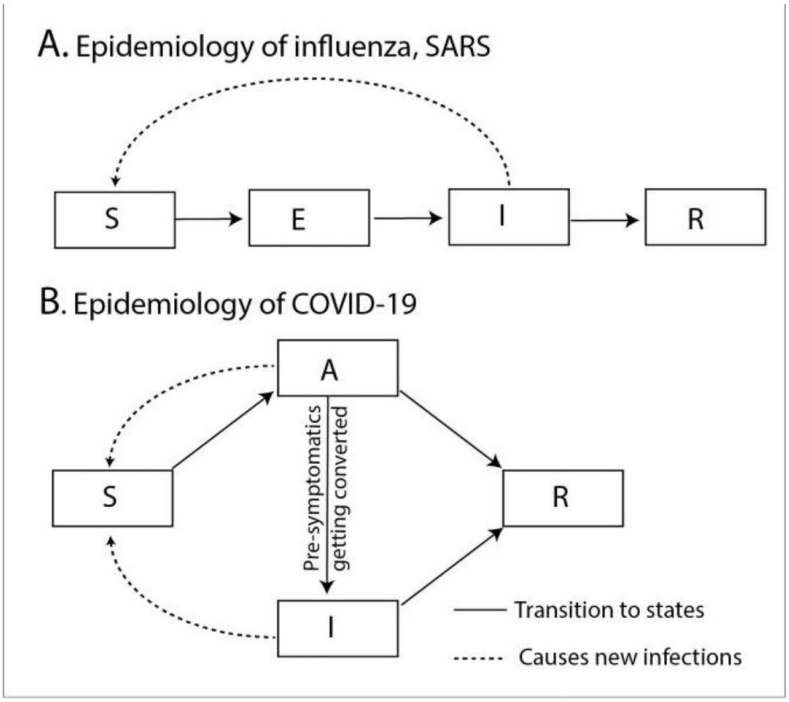

Figure 2. Schematic illustrating the difference between the standard SEIR model and the SAIR model used in this work. A typical SEIR model assumes a framework of serial, directed transitions across the intermediate health states of the individuals. In this framework, the infections are caused when a susceptible person comes in contact with a person deemed to be infected person on the basis of the symptoms (I). However, after this contact, with a certain likelihood the person remains in a pre-symptomatic intermediate state or the exposed individual (E), that is not contagious, before transitioning to a contagious and symptomatic state (I). While this framework is acceptable for influenza or SARS, the epidemiology of COVID-19 is such that there is an alternative pathway between the susceptible (S) and the recovered states (R) which passes through asymptomatic individuals (estimated to be around 86%), [3] who never show any symptoms but carry enough viral load to infect others. Thus a model for COVID-19 should consider two parallel pathways of infection (Figure 2B).

QUANTITATIVE EVALUATION AND PROGRESS OF OLFACTORY DYSFUNCTION IN COVID-19

Ugurlu BN, Akdogan O, Yilmaz YA, Yapar D, Aktar Ugurlu G, Yerlikaya HS, Aslan Felek S.. Eur Arch Otorhinolaryngol. 2021 Jan 1. doi: 10.1007/s00405-020-06516-4. Online ahead of print.
Level of Evidence: 3 - Local non-random sample

BLUF

Otolaryngologists, pulmonologists, and infectious disease physicians from the Hitit University Erol Olçok Training and Research Hospital in Çorum, Turkey used the Brief Smell Identification Test (BSIT) to evaluate olfactory function in 104 patients hospitalized with COVID-19. They found 40.3% (n=42) had some degree of olfactory dysfunction (mild: 52.4%, moderate: 31%, severe: 16.7%)(Figure 1), with 85.7% reporting full recovery at three months. Because 40% reported olfactory dysfunction as their first symptom, authors suggest assessment of olfactory function should occur early in the diagnosis of suspected COVID-19.

ABSTRACT

PURPOSE: Since many different rates have been reported in the literature and the studies conducted are mostly based on the patient anamnesis, it was aimed to analyze the olfactory dysfunction in Coronavirus Disease 2019 (COVID-19) quantitatively and to reveal its progress by time. METHODS: Patients who described new-onset olfactory dysfunction, who were treated in the COVID-19 departments of our hospital and whose PCR tests demonstrated SARS-CoV-2 presence were included in the study and they were investigated prospectively. Clinical information of all the patients was taken and the levels of olfactory function were detected using the Brief Smell Identification Test (BSIT). Scores equal to or below 8 are considered as olfactory dysfunction. Patients who were followed up for 3 months were reevaluated with the BSIT test at the end of the third month and the progression of the symptom was investigated. RESULTS: The mean BSIT test score of the 42 patients (23 female patients, 19 male patients, mean age: 41.2 +- 14.6) was 5.2 +- 2.2. There was severe olfactory dysfunction in 16.7% of the patients (0-2 points), moderate olfactory dysfunction in 31% (3-5 points), and mild olfactory dysfunction in 52.4% (6-8 points). After a follow-up for 3 months, full recovery was observed in 36 patients (85.7%) and the mean test score rose to 9.9 +- 1.8. Although olfactory dysfunction persisted in 6 patients, an elevation in test scores was noted. Olfactory dysfunction was the first symptom in 17 patients (40%) and the other symptoms occurred after 2 days (1-6) on average. CONCLUSION: We investigated olfactory dysfunction caused by COVID-19 using BSIT, and found a high rate of moderate-mild level symptoms with a high level of recovery in the 3-month follow-up. The finding revealing that olfactory dysfunction was the first symptom in 40% of the patients suggests the importance of inquiry on olfactory functions for the early diagnosis of the disease.

PHOSPHATIDYLSERINE INSIDE OUT: A POSSIBLE UNDERLYING MECHANISM IN THE INFLAMMATION AND COAGULATION ABNORMALITIES OF COVID-19

Argañaraz GA, Palmeira JDF, Argañaraz ER.. Cell Commun Signal. 2020 Dec 27;18(1):190. doi: 10.1186/s12964-020-00687-7.
Level of Evidence: 5 - Review / Literature Review

BLUF

In this review, authors from the Laboratory of Molecular Neurovirology at the University of Brasília, Brazil detail the pathophysiology and biochemical pathways of coagulation and endothelial inflammation in the setting of SARS-CoV-2 (Figure 1). They propose the exposure of phosphatidylserine (PtdSer) on infected endothelial cell membranes may be an underlying mechanism of activation of the coagulation cascade, with the subsequent decreased activity of ADAMTS13 and accumulation of vWF, leading to a hyper-coagulable state. The authors highlight this potential mechanism for future inquiry and therapeutic targeting and state the importance of monitoring COVID-19 patients for coagulation complications.

ABSTRACT

The rapid ability of SARS-CoV-2 to spread among humans, along with the clinical complications of coronavirus disease 2019-COVID-19, have represented a significant challenge to the health management systems worldwide. The acute inflammation and coagulation abnormalities appear as the main causes for thousands of deaths worldwide. The intense inflammatory response could be involved with the formation of thrombi. For instance, the presence of uncleaved large multimers of von Willebrand (vWF), due to low ADAMTS13 activity in plasma could be explained by the inhibitory action of pro-inflammatory molecules such as IL-1beta and C reactive protein. In addition, the damage to endothelial cells after viral infection and/or activation of endothelium by pro-inflammatory cytokines, such as IL-1beta, IL-6, IFN-gamma, IL-8, and TNF-alpha induces platelets and monocyte aggregation in the vascular wall and expression of tissue factor (TF). The TF expression may culminate in the formation of thrombi, and activation of cascade by the extrinsic pathway by association with factor VII. In this scenario, the phosphatidylserine-PtdSer exposure on the outer leaflet of the cell membrane as consequence of viral infection emerges as another possible underlying mechanism to acute immune inflammatory response and activation of coagulation cascade. The PtdSer exposure may be an important mechanism related to ADAM17-mediated ACE2, TNF-alpha, EGFR and IL-6R shedding, and the activation of TF on the surface of infected endothelial cells. In this review, we address the underlying mechanisms involved in the pathophysiology of inflammation and coagulation abnormalities. Moreover, we introduce key biochemical and pathophysiological concepts that support the possible participation of PtdSer exposure on the outer side of the SARS-CoV-2 infected cells membrane, in the pathophysiology of COVID-19. Video Abstract.

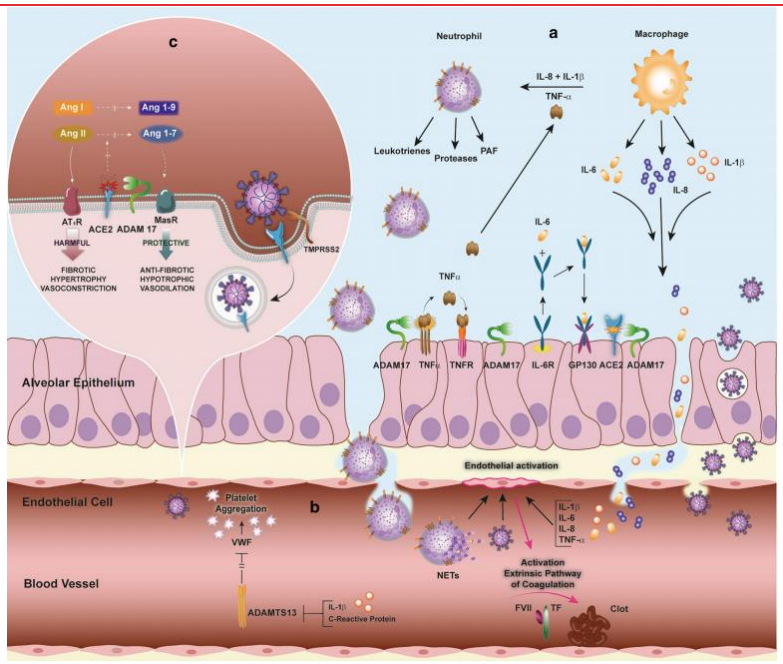

Figure 1. Molecular mechanisms involved in the acute infammation and coagulation abnormalities of COVID-19. a The SARS-CoV-2 infection triggers an infammatory cellular infltrate in the alveolar lumen releases toxic molecules by macrophages and neutrophils, such as IL-1β, IL-8, IL-6 and TNF-α. The cytokines storm lead to difuse alveolar damage, pulmonary oedema. b The damage and /or activation of blood vessels endothelium by viral infection and pro-infammatory cytokines respectively induce platelet and monocyte aggregation in the vascular wall. These events are accompanied by increased expression of the tissue factor (TF) leading to activation of extrinsic pathway coagulation cascade culminating with the thrombi formation. Moreover, the thrombotic microangiopathy, may also be consequence of uncleaved large multimers of VWF, due to a decrease in the plasma levels of ADAMTS13. c Finally, as consequence of blood vessels endothelium viral infection, ACE2 is internalized, and sheddase activity of ADAM17 is increased. The ACE2 downmodulation and TNF-α and IL-6R release exacerbates the imbalance of RAS, leading to increase
infammation. The virus-mediated PtdSer exposure on the outer leafet of the cell membrane emerge as an underlying mechanism to activate TF and extrinsic pathway coagulation cascade and infammation (not shown).

CRITICAL CARE

BRACHIAL PLEXUS NEUROPATHIES DURING THE COVID-19 PANDEMIC: A RETROSPECTIVE CASE SERIES OF 15 PATIENTS IN CRITICAL CARE

Miller C, O'Sullivan J, Jeffrey J, Power D.. Phys Ther. 2021 Jan 4;101(1):pzaa191. doi: 10.1093/ptj/pzaa191.
Level of Evidence: 4 - Case-series

BLUF

Physiotherapists from Queen Elizabeth Hospital in Birmingham, United Kingdom assessed the prevalence of nerve injuries in 114 patients hospitalized with COVID-19 who underwent long periods of proning between March and June 2020. They found 30 total peripheral nerve injuries in 21 limbs, most commonly ulnar (12/30) and brachial plexus (10/30). The authors conclude that prone positioning can cause neuropathies and provide a guidance document to aid nonspecialists in screening for injury and optimizing patient positioning (Figure).

ABSTRACT

OBJECTIVE: The use of the prone position to treat patients with COVID-19 pneumonia who are critically ill and mechanically ventilated is well documented. This case series reports the location, severity, and prevalence of focal peripheral nerve injuries involving the upper limb identified in an acute COVID-19 rehabilitation setting. The purpose of this study was to report observations and to explore the challenges in assessing these patients. METHODS: Participants were patients with suspected peripheral nerve injuries following discharge from COVID-19 critical care who were referred to the peripheral nerve injury multidisciplinary team. Data were collected retrospectively on what peripheral neuropathies were observed, with reference to relevant investigation findings and proning history. RESULTS: During the first wave of the COVID-19 pandemic in the United Kingdom, 256 patients were admitted to COVID-19 critical care of Queen Elizabeth Hospital, Birmingham, United Kingdom. From March to June 2020, a total of 114 patients required prone ventilation. In this subgroup, a total of 15 patients were identified with clinical findings of peripheral nerve injuries within the upper limb. In total, 30 anatomical nerve injuries were recorded. The most commonly affected nerve was the ulnar nerve (12/30) followed by the cords of the brachial plexus (10/30). Neuropathic pain and muscle wasting were identified, signifying a high-grade nerve injury. CONCLUSION: Peripheral nerve injuries can be associated with prone positioning on intensive care units, although other mechanisms, such as those of a neuroinflammatory nature, cannot be excluded. IMPACT: Proning-related upper limb peripheral nerve injuries are not discussed widely in the literature and could be an area of further consideration when critical care units review their proning protocols. Physical therapists treating these patients play a key part in the management of this group of patients by optimizing the positioning of patients during proning, making early identification of peripheral nerve injuries, providing rehabilitation interventions, and referring to specialist services if necessary. LAY SUMMARY: During the COVID-19 pandemic, patients who are very ill can be placed for long periods of time on their stomach to improve their chances of survival. The potential consequences of prolonged time in this position are weakness and pain in the arms due to potential nerve damage. There are some recommended treatments to take care of these problems.

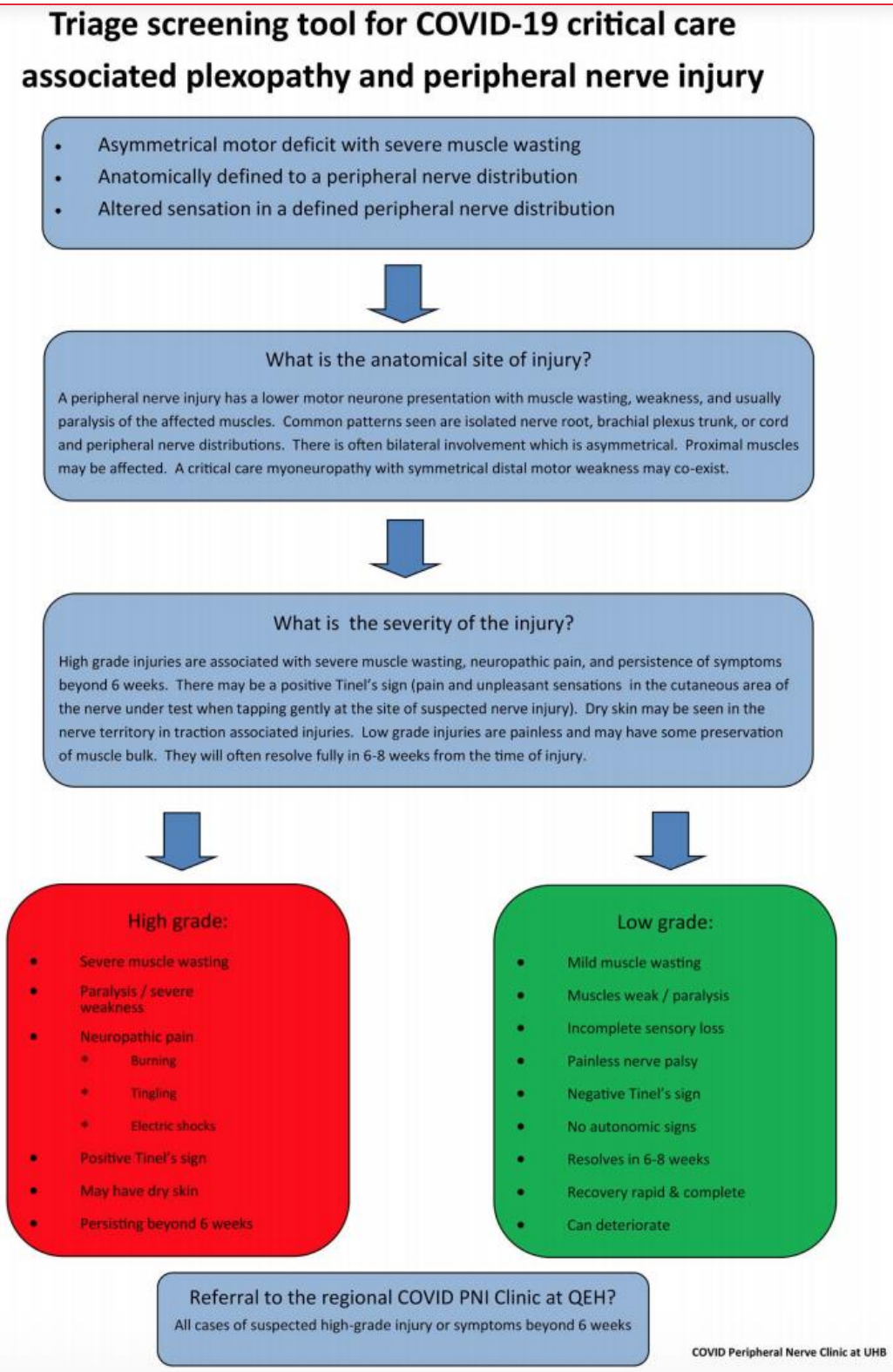

Figure. Screening tool for COVID-19 critical care–associated plexopathy. PNI; QEH = Queen Elizabeth Hospital (Birmingham, UK).

MAINTAINING MOBILITY IN A PATIENT WHO IS PREGNANT AND HAS COVID-19 REQUIRING EXTRACORPOREAL MEMBRANE OXYGENATION: A CASE REPORT

Mark A, Crumley JP, Rudolph KL, Doerschug K, Krupp A.. Phys Ther. 2021 Jan 4;101(1):pzaa189. doi: 10.1093/ptj/pzaa189.
Level of Evidence: 5 - Case Report

BLUF

A team of physicians and nurses from the University of Iowa present the case of a 27-year-old pregnant female with COVID-19 requiring venovenous extracorporeal membrane oxygenation (ECMO) for 9 days. The physical therapists initiated early mobility with sitting on edge of the bed, standing on day 5 and ambulation by day 9 of ECMO (Table). She discharged on day 14 of hospitalization with recommended outpatient physical therapy. Authors suggest similar creative, multidisciplinary approaches to facilitate early mobility in COVID-19 patients on ECMO can ensure safe restoration of their physical function.

ABSTRACT

OBJECTIVE: Mobilization while receiving life support interventions, including mechanical ventilation and extracorporeal membrane oxygenation (ECMO), is a recommended intensive care unit (ICU) intervention to maintain physical function. The purpose of this case report is to describe a novel approach to implementing early mobility interventions for a patient who was pregnant and receiving ECMO while continuing necessary infectious disease precautions because of diagnosed coronavirus disease-19 (COVID-19). METHODS: A 27-year-old woman who was pregnant was admitted to the ICU with COVID-19 and rapidly developed acute respiratory failure requiring 9 days of ECMO support. After a physical therapist consultation, the patient was standing at the bedside by hospital day 5 and ambulating by hospital day 9. RESULTS: The patient safely participated in physical therapy during ICU admission and was discharged to home with outpatient physical therapy follow-up after 14 days of hospitalization. CONCLUSION: Early mobility is feasible during ECMO with COVID-19, and active participation in physical therapy, including in-room ambulation, may facilitate discharge to home. Innovative strategies to facilitate routine activity in a patient who is critically ill with COVID-19 require an established and highly trained team with a focus on maintaining function. IMPACT: Early mobility while intubated, on ECMO, and infected with COVID-19 is feasible while adhering to infectious disease precautions when it is performed by an experienced interdisciplinary team.

Table. Major Medical Events, Safety Assessment, and Activity Interventions[a]

Hospital Day	Major Medical Events	Safety Assessment		Activity Intervention	Response to Progressive Mobility	Personnel Present in Room
		Respiratory	Neurologic and Sedative Infusions			
1	At admission: endotracheal intubation, VV ECMO cannulation	Mode = VC Fio_2 = 0.60 RR = 16 PEEP = 8	SAS = 2 Fentanyl, Propofol	Bed rest		RN
2	Sedation weaning	Mode = VC Fio_2 = 0.40 RR = 16 PEEP = 10	SAS = 3 Fentanyl, Propofol	PT consult PROM performed by RN		RN, ECMO specialist
3	Sedation weaning Adjustment in ECMO parameters	Mode = VC Fio_2 = 0.40 RR = 16 PEEP = 12	SAS = 3 Fentanyl, Propofol	PROM performed by RN		RN, ECMO specialist
4	SAT Ventilator dyssynchrony	Mode = VC Fio_2 = 0.30 RR = 10 PEEP = 16	SAS = 3 or 4 Fentanyl, Dexmedetomidine	PROM performed by RN, cardiac chair position in bed (head of bed 45°)	Stable vital signs in cardiac chair mode	RN, ECMO specialist
5	SAT	Mode = VC Fio_2 = 0.30 RR = 10 PEEP = 16	SAS = 3 or 4 Fentanyl, Dexmedetomidine CAM-ICU positive for delirium	AROM exercises in supine position: ankle pumps, 10 reps; heel slides, 10 reps; short-arc quad exercises, 10 reps; shoulder flexion, 10 reps; elbow flexion and extension, 10 reps; all exercises performed bilaterally Sit-to-stand at bedside, 2 reps (60 s of rest between reps)	Patient's extremity strength improved with repetitions (MRC 1/5→3/5) Spo_2 = 93–100% Peak HR = 100 bpm BP = 113/60 (supine) and 113/80 (standing) Total treatment time = 55 min	PT, RN, ECMO specialist, RT
6	SAT Consent for preterm labor	Mode = VC Fio_2 = 0.30 RR = 10 PEEP = 16	SAS = 3 or 4 Fentanyl, Dexmedetomidine	AROM exercises performed by RN in supine and cardiac chair positions	Out-of-bed activity held	RN, ECMO specialist
7	SAT Episode of hypertension	Mode = VC Fio_2 = 0.30 RR = 10 PEEP = 16	SAS = 3 or 4 Dexmedetomidine	AROM exercises performed by RN Sit-to-stand at bedside, 1 rep	Improved sit-to-stand strength and standing balance reported by RN	RN, ECMO specialist, RT
8	First trial off ECMO	Mode = VC Fio_2 = 0.30 RR = 26 PEEP = 14	SAS = 4 Dexmedetomidine	Supine exercises: AROM heel slides, 10 reps; hip/knee extension with manual resistance by PT, 10 reps; ankle pumps with manual plantar flexion resistance by PT, 10 reps; all exercises performed bilaterally Standing at bedside, 3 reps (60 s of rest between reps), with marching for 30 s and side-stepping at bedside on final attempt	Extremity strength 4/5 bilaterally in lower extremities with supine exercise Best standing attempt = 60 s Spo_2 = 97–100% Peak HR = 90 bpm BP = 116/65 (supine) and 75/49 (standing) Total treatment time = 39 min	PT, RN, ECMO specialist, RT, OT
9	ECMO decannulation	Mode = VC Fio_2 = 0.30 RR = 26 PEEP = 14	SAS = 4 Dexmedetomidine CAM-ICU negative for delirium	Supine exercises: AROM heel slides, 10 reps; hip/knee extension with manual resistance by PT, 10 reps; ankle pumps with manual plantar flexion resistance by PT, 10 reps; all exercises performed bilaterally Walking in room, ~3 m (10 ft), 2 reps (2 min of rest between reps)	Extremity strength 4/5 bilaterally in lower extremities with supine exercise Spo_2 = 92–100% Peak HR = 87 bpm BP = 120/62 (supine) and 96/62 (after walking) Total treatment time = 45 min	PT (2), RN, ECMO specialist

(Continued)

Table : "Major Medical Events, Safety Assessment, and Activity Interventions".

Table. Continued.

Hospital Day	Major Medical Events	Safety Assessment: Respiratory	Safety Assessment: Neurologic and Sedative Infusions	Activity Intervention	Response to Progressive Mobility	Personnel Present in Room
10	Extubation to high-flow nasal cannula Respiratory distress in afternoon	40 L/min Fio_2 = 0.35	SAS = 4	Therapy by PT/OT held because of tachycardia, tachypnea, and respiratory distress after extubation		RN
11	Supplemental O_2 weaning	40 L/min Fio_2 = 0.30	SAS = 4	Morning physical therapy: Supine exercises: AROM heel slides, 10 reps; hip/knee extension with manual resistance by PT, 10 reps; ankle pumps with manual plantar flexion resistance by PT, 10 reps; all exercises performed bilaterally Walking ~6 m (20 ft) continuously (60 s of rest between supine exercise and walking) Afternoon physical therapy: Walking ~12 m (40 ft) continuously Occupational therapy: Upper extremity resistance band exercise; coping techniques for anxiety; breathing/relaxation exercises; ADL training	Extremity strength 4/5 bilaterally in lower extremities with supine exercise Spo_2 = 97–100% Peak HR = 129 bpm BP = 126/68 (supine) and 134/60 (after walking) Total treatment time = 41 min	PT, OT
12	Weaned off O_2	Room air	SAS = 4	Morning physical therapy: Walking ~6 m (20 ft) continuously Toileting tasks Resistance band exercises: seated knee extension, 10 reps; seated hip abduction, 10 reps; seated hip/knee extension against band, 10 reps; seated ankle pumps against band, 10 reps (30 s of rest between exercises) Afternoon physical therapy: Walking ~18 m (60 ft) continuously Single-stair training, 4 reps (60 s of rest between walking and stair training) Issued walker, written home exercise program of morning exercises to perform (10 reps, 3 times/d, independently), and resistance band for expected weekend discharge Occupational therapy: Upper extremity resistance band exercise review Discharge planning	Spo_2 = 97–99% Peak HR = 116 bpm BP = 119/58 (after walking) Total treatment time = 39 min	PT, OT
13		Room air	SAS = 4	Ambulation in room Independent resistance band exercise	Spo_2 = 97–99%	RN
14	Discharged to home	Room air	SAS = 4	Ambulation in room Independent resistance band exercise	Spo_2 = 97–99%	RN

[a] ADL = activities of daily living; AROM = active range of motion; BP = blood pressure; bpm = beats per minute; CAM-ICU = Confusion Assessment Method for the intensive care unit; ECMO = extracorporeal membrane oxygenation; Fio_2 = fraction of inspired oxygen; HR = heart rate; MRC = Medical Research Council Scale for Muscle Strength; OT = occupational therapist; PEEP = positive end expiratory pressure; PROM = passive range of motion; PT = physical therapist; rep = repetition; reps = repetitions; RN = registered nurse; RR = respiratory rate; RT = respiratory therapist; SAS = Riker Sedation-Agitation Scale score; SAT = spontaneous awakening trial; Spo_2 = peripheral oxygen saturation; VC = volume control; VV ECMO = venovenous extracorporeal membrane oxygenation.

Table(continued): "Major Medical Events, Safety Assessment, and Activity Interventions".

THE ASSOCIATION OF LOW MOLECULAR WEIGHT HEPARIN USE AND IN-HOSPITAL MORTALITY AMONG PATIENTS HOSPITALIZED WITH COVID-19

Shen L, Qiu L, Liu D, Wang L, Huang H, Ge H, Xiao Y, Liu Y, Jin J, Liu X, Wang DW, Peterson ED, He B, Zhou N.. Cardiovasc Drugs Ther. 2021 Jan 4. doi: 10.1007/s10557-020-07133-3. Online ahead of print.
Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

A team of cardiologists and pharmacists from hospitals in Shanghai and Wuhan, China assessed the association between mortality in hospitalized COVID-19 patients (n=535, Table 1) and low molecular weight heparin (LMWH) use between January 26-March 26, 2020. They found overall adjusted odds ratio for mortality was lower in the LMWH-users vs non-users (0.20; 95% CI, 0.09-0.46), specifically in severe (0.08; 95% CI, 0.01–0.62) and critically ill cases (0.32; 95% CI ,0.10–0.996) (severity defined in summary)(Table 3). Authors suggest LMWH appears correlated with a survival benefit in hospitalized COVID-19 patients, especially those severely and critically ill.

SUMMARY

The authors defined the following patient groups:

Severe, if at least one of the following:
(1) shortness of breath, RR ≥ 30 times/min;
(2) oxygen saturation ≤ 93%;
(3) alveolar oxygen partial pressure/fraction of inspiration O2 (PO2/FiO2) ≤ 300 mmHg; and
(4) patients whose pulmonary imaging showed significant progression of lesion > 50% within 24–48 h."

Critically ill if respiratory failure requiring mechanical ventilation, septic shock, or combined with other organ failure needing intensive care unit (ICU) monitoring and treatment.

Mild/moderate patients had none of the above characteristics, with or without a symptom of pneumonia.

ABSTRACT

PURPOSE: To determine the association between low molecular weight heparin (LMWH) use and mortality in hospitalized COVID-19 patients. METHODS: We conducted a retrospective study of patients consecutively enrolled from two major academic hospitals exclusively for COVID-19 in Wuhan, China, from January 26, 2020, to March 26, 2020. The primary outcome was adjusted in-hospital mortality in the LMWH group compared with the non-LMWH group using the propensity score. RESULTS: Overall, 525 patients with COVID-19 enrolled with a median age of 64 years (IQR 19), and 49.33% men. Among these, 120 (22.86%) were treated with LMWH. Compared with the non-LMWH group, the LMWH group was more likely to be older and male; had a history of hypertension, diabetes, coronary heart disease (CHD), or stroke; and had more severe COVID-19 parameters such as higher inflammatory cytokines or D-dimer. Compared with non-LMWH group, LMWH group had a higher unadjusted in-hospital mortality rate (21.70% vs. 11.10%; p = 0.004), but a lower adjusted mortality risk (adjusted odds ratio [OR], 0.20; 95% CI, 0.09-0.46). A propensity score-weighting analysis demonstrated similar findings (adjusted OR, 0.18; 95% CI, 0.10-0.30). Subgroup analysis showed a significant survival benefit among those who were severely (adjusted OR, 0.07; 95% CI, 0.02-0.23) and critically ill (adjusted OR, 0.32; 95% CI, 0.15-0.65), as well as among the elderly patients' age > 65, IL-6 > 10 times upper limit level, and D-dimer > 5 times upper limit level. CONCLUSIONS: Among hospitalized COVID-19 patients, LMWH use was associated with lower all-cause in-hospital mortality than non-LMWH users. The survival benefit was particularly significant among more severely ill patients.

Table 1 Baseline characteristics of the study population according to LMWH use

From: The Association of Low Molecular Weight Heparin Use and In-hospital Mortality Among Patients Hospitalized with COVID-19

Variables	All (*N* = 525)	On LMWH (*N* = 120)	Non-LMWH (*N* = 405)	*p*
Age (years)	64 (19)	70 (16.75)	63 (21)	0
Sex	–	–	–	0.105
Male	259 (49.33)	67 (55.83)	192 (47.41)	
Female	266 (50.67)	53 (44.17)	213 (52.59)	
Hypertension (%)	196 (37.33)	64 (53.33)	132 (32.59)	0.699
DM (%)	93 (17.71)	29 (24.17)	64 (15.8)	0.375
COPD (%)	29 (5.52)	5 (4.17)	24 (5.93)	0.047
CHD (%)	55 (10.48)	18 (15)	37 (9.14)	0.884
Stroke (%)	33 (6.29)	12 (10)	21 (5.19)	0.816
Liver disease (%)	4 (0.76)	0 (0)	4 (0.99)	1
Tumor (%)	9 (1.71)	1 (0.83)	8 (1.98)	0.248
ALT (u/l)	24 (26)	26 (28.75)	23 (25)	0.07
AST (u/l)	27 (21)	31.5 (29)	26 (19)	0.004
Creatinine (μmol/l)	68 (30.18)	71 (30.75)	67 (28.25)	0.32
Hb (g/l)	125 (27.75)	125 (27.5)	126 (27)	0.463
WBC (× 10^9/l)	6.46 (3.92)	8 (4.34)	6.01 (3.49)	0
PLT(× 10^9/l)	225 (126)	199 (122)	227.5 (121)	0.094
hs-CRP (mg/l)	26.35 (74.55)	63.5 (100.01)	18.4 (59.75)	0
IL-6 (pg/ml)	12.11 (40.29)	25.2 (59.27)	7.89 (34.08)	0
PCT (ng/ml)	0.08 (0.17)	0.14 (0.24)	0.07 (0.11)	0
D-dimer (μg/ml)	1.05 (1.73)	2.49 (4.29)	0.83 (1.34)	0
Invasive ventilation (%)	57 (10.86)	40 (33.33)	17 (4.2)	0.178
Non-invasive ventilation (%)	118 (22.48)	49 (40.83)	69 (17.04)	0.624
ECMO (%)	2 (0.38)	2 (1.67)	0 (0%)	1
Aspirin (%)	40 (7.62)	17 (14.17)	23 (5.68)	0.002
Clopidogrel (%)	24 (4.57)	11 (9.17)	13 (3.21)	0.006
Antiviral treatment (%)	274 (52.19)	108 (90.00)	166 (40.99)	1
Immunological treatment (%)	171 (32.57)	76 (63.33)	95 (23.46)	0.0001
Severity classification				0
Mild/moderate	251 (47.81)	12 (10)	239 (59.01)	
Severe	185 (35.24)	41 (34.17)	144 (35.56)	
Critically ill	89 (16.95)	67 (55.83)	22 (5.43)	

DM diabetes mellitus, *CHD* coronary heart disease, *ALT* alanine aminotransferase, *AST* aspartate transaminase, *Hb* hemoglobin, *WBC* white blood cell, *PLT* platelet, *CRP* C-reactive protein, *IL-6* interleukin-6, *PCT* procalcitonin, *BiPAP* bilevel positive airway pressure, *ECMO* extracorporeal membrane oxygenation

Continuous variables are presented as median (IQR), categorical variables are presented as n percentage

Table 3 Adjusted in-hospital mortality rate compared by LMWH versus non-LMWH, before and after propensity score weighting, respectively

From: The Association of Low Molecular Weight Heparin Use and In-hospital Mortality Among Patients Hospitalized with COVID-19

	Unweighted		Weighted	
Outcomes	Adjusted OR (95% CI)	*p* Value	Adjusted OR (95% CI)	*p* Value
In-hospital mortality	0.20 (0.09–0.46)	$p = 0.001$	0.18 (0.10–0.30)	$p = 0$
Mild/moderate	N/A	$p = 1$	N/A	$p = 1$
Severe	0.08 (0.01–0.62)	$p = 0.016$	0.07 (0.02–0.23)	$p = 0$
Critically ill	0.32 (0.10–0.996)	$p = 0.049$	0.315 (0.15–0.65)	$p = 0.002$

A PARADIGM SHIFT IN THE DELIVERY OF PHYSICAL THERAPY SERVICES FOR CHILDREN WITH DISABILITIES IN THE TIME OF THE COVID-19 PANDEMIC

Rao PT.. Phys Ther. 2021 Jan 4;101(1):pzaa192. doi: 10.1093/ptj/pzaa192.
Level of Evidence: 5 - Opinion

BLUF

A physical therapist at the Manipal Hospital Department of Physiotherapy in Karnataka, India discusses the need for physical therapy services to adapt to the COVID-19 pandemic. They argue effective care will become home-based and family-centered, engaging with new technologies such as smartphone apps, incorporating telerehabilitation, and utilizing community healthcare workers (Figure). The author suggests that refocusing and implementing these methods could allow broader access to crucial therapies, particularly benefiting children with disabilities who cannot currently access physical therapy facilities and are more negatively impacted by the changes to lifestyle and home isolation.

FIGURES

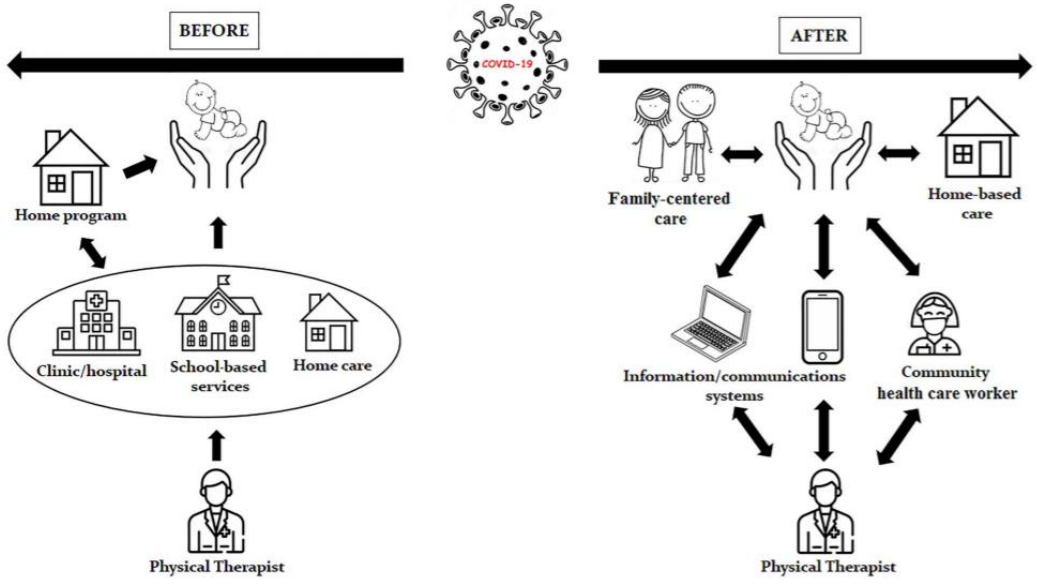

Figure. Framework of care for children with disabilities.

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