The Daily COVID-19 Literature Surveillance Summary

February 25, 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

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EXECUTIVE SUMMARY

Transmission & Prevention

- Researchers in Shanghai, China conducted an on-site analysis of COVID-19 surface contamination using a real-time nucleic acid extraction-free isothermal amplification kit. They collected 31 samples from 7 sites within the wards of the Chengdu Center of Disease Control and found a high transmissibility from positive patients, most concentrated on ECG fingertips, bedrails, remote controls, and cupboards, in decreasing order. The findings suggest that paying extra attention to commonly touched surfaces when cleaning hospital rooms may have a greater impact on preventing nosocomial COVID-19 transmission.

- Researchers from Emory University in conjunction with the CDC investigated the extent of aerosolized SARS-CoV-2 particles, by using 8 National Institute for Occupational Safety and Health (NIOSH) BC 251 two-stage cyclone samples in six units throughout a tertiary care hospital in Atlanta, Georgia. They collected a total of 528 aerosolized samples from medical units, ICUs, inpatient hallways, nursing stations and visitor corridors, all of which were negative by rRT-PCR for SARS-CoV-2. The authors note their promising results suggest a decreased likelihood of transmission as compared to previously thought, however, they acknowledge there is still much to be learned about COVID-19, and every precautionary step should continue to be taken to decrease exposure of health care personnel.

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CLIMATE

GLOBAL

QUALITY ADJUSTED LIFE YEARS IN THE TIME OF COVID-19

Hall J, Viney R.. Aust Health Rev. 2021 Jan 29. doi: 10.1071/AH21010. Online ahead of print.
Level of Evidence: 5 - Expert Opinion

BLUF

Two professors from the Centre for Health Economics Research and Evaluation in Australia describe how the severity of the COVID-19 pandemic has changed the assessment of economic evaluation and cost effectiveness of vaccines by the QALY (quality adjusted life year) metric. Because of the economic and social impact of this pandemic, they state that the stakes of not controlling the pandemic are too high, and therefore, these new vaccines are not undergoing the same rigorous economic evaluation as other vaccines. This has led to the country being hesitant about allowing vaccines into the country.

ABSTRACT

The quality adjusted life year (QALY) as a basis of valuing additional expenditure on health is widely accepted. Although early in the COVID-19 pandemic, several commentators called for a similar approach in resolving trade-offs between economic activity and reducing the burden of COVID-19, this has not occurred. The value of a QALY has not been used to deny all intervention, as the rule of rescue attests. Further, while there was no other way of managing the pandemic, there were other means available to mitigate the economic losses. Now that vaccine programs have commenced in several countries, it is interesting to consider whether economic evaluation should now be applied. However, the recognised complexities of the evaluation of vaccines, plus the challenge of measuring opportunity costs in the face of an economic recession and the severity of the consequences of an outbreak even though the probability of transmission is exceedingly low, mean its use will be restricted. COVID-19 has changed everything, even the way we should think about economic evaluation.

DEVELOPMENTS IN TRANSMISSION & PREVENTION

DURATION OF CULTURABLE SARS-COV-2 IN HOSPITALIZED PATIENTS WITH COVID-19

Kim MC, Cui C, Shin KR, Bae JY, Kweon OJ, Lee MK, Choi SH, Jung SY, Park MS, Chung JW.. N Engl J Med. 2021 Jan 27. doi: 10.1056/NEJMc2027040. Online ahead of print.
Level of Evidence: 4 - Case-series

BLUF

In this letter to the editor, the authors from Korea University College of Medicine and Chung-Ang University Hospital, Seoul, South Korea, briefly outline results from their recent study reporting the duration of measurable SARS-CoV-2 cultured in COVID-19 patients admitted to Chung-Ang University Hospital between February - June 2020. They found 33% of patients had culturable SARS-CoV-2, with incidence decreasing as time from symptom onset increased (Figure 1), providing additional data to inform isolation period guidelines for COVID-19 patients as the pandemic continues.

FIGURES

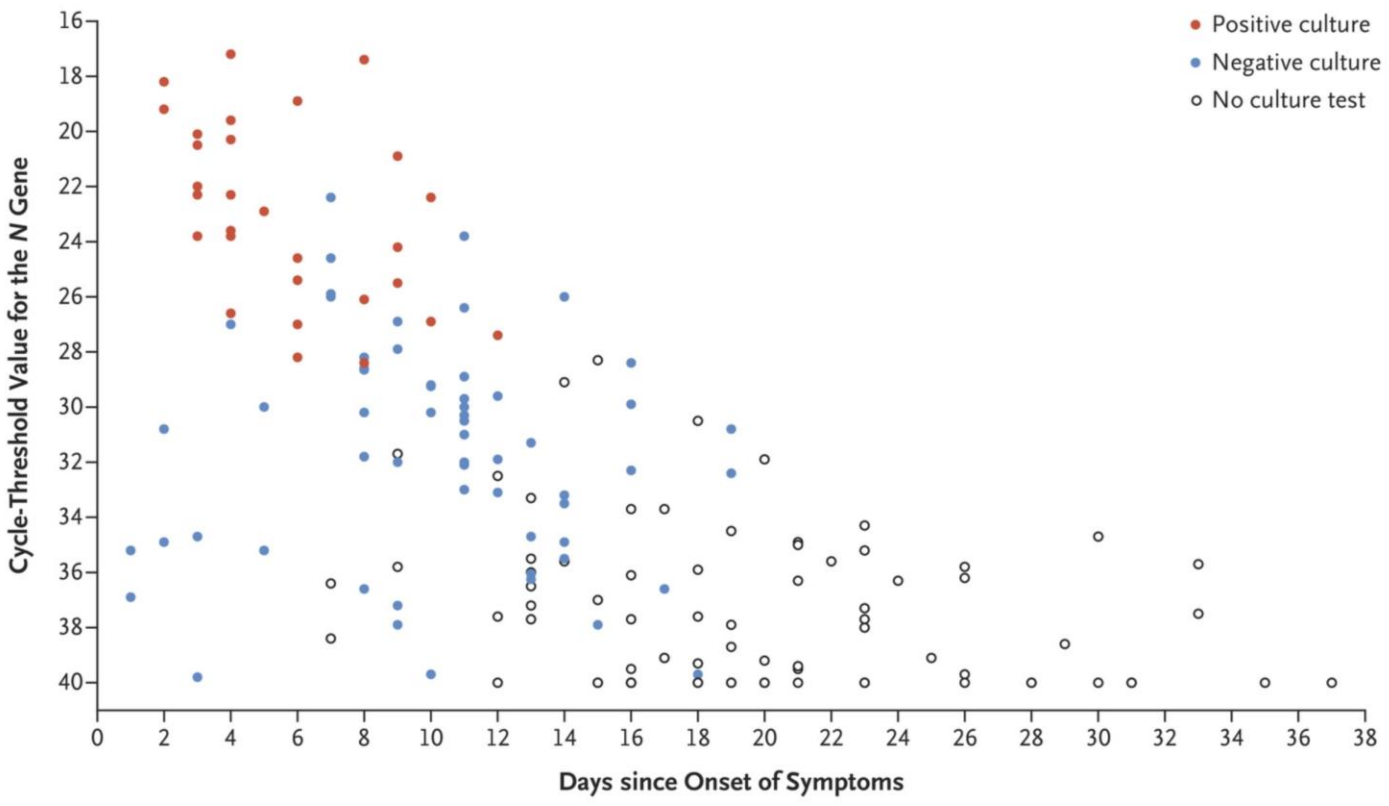

Figure 1. Timing of Presence or Absence of Viable SARS-CoV-2 on Viral Culture and Cycle-Threshold Values for 165 Serial Samples Obtained from 21 Consecutive Patients Hospitalized with Covid-19.

ON-SITE ANALYSIS OF COVID-19 ON THE SURFACES IN WARDS

Wan B, Zhang X, Luo D, Zhang T, Chen X, Yao Y, Zhao X, Lei L, Liu C, Zhao W, Zhou L, Ge Y, Mao H, Liu S, Chen J, Cheng X, Zhao J, Sui G.. Sci Total Environ. 2021 Jan 20;753:141758. doi: 10.1016/j.scitotenv.2020.141758. Epub 2020 Aug 18.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Researchers in Shanghai, China conducted an on-site analysis of COVID-19 surface contamination using a real-time nucleic acid extraction-free isothermal amplification kit. They collected 31 samples from 7 sites within the wards of the Chengdu Center of Disease Control from March 18 - April 28, 2020 and found a high transmissibility from positive patients, most concentrated on ECG fingertips, bedrails, remote controls, and cupboards, in decreasing order. The findings suggest that paying extra attention to commonly touched surfaces when cleaning hospital rooms may have a greater impact on preventing nosocomial COVID-19 transmission.

ABSTRACT

SARS-Cov-2 has erupted across the globe, and confirmed cases of COVID-19 pose a high infection risk. Infected patients typically receive their treatment in specific isolation wards, where they are confined for at least 14 days. The virus may contaminate any surface of the room, especially frequently touched surfaces. Therefore, surface contamination in wards should be monitored for disease control and hygiene purposes. Herein, surface contamination in the ward was detected on-site using an RNA extraction-free rapid method. The whole detection process, from surface sample collection to readout of the detection results, was finished within 45 min. The nucleic acid extraction-free method requires minimal labor. More importantly, the tests were performed on-site and the results were obtained almost in real-time. The test confirmed that 31 patients contaminated seven individual sites. Among the sampled surfaces, the electrocardiogram fingertip presented a 72.7% positive rate, indicating that this surface is an important hygiene site. Meanwhile, the bedrails showed the highest correlation with other surfaces, so should be detected daily. Another surface with high contamination risk was the door handle in the bathroom. To our knowledge, we present the first on-site analysis of COVID-19 surface contamination in wards. The results and applied technique provide a potential further reference for disease control and hygiene suggestions.

COVID-19 RATES INCREASED WHERE IN-PERSON COLLEGE CLASSES WERE HELD

Kuehn BM.. JAMA. 2021 Feb 23;325(8):714. doi: 10.1001/jama.2021.0621.
Level of Evidence: 5 - Review / Literature Review

BLUF

A JAMA reporter details the steep increase in the regional incidence of COVID-19 when colleges went back to in-person classes last fall as reported by the CDC, stating cases in 18 to 22 year-olds increased by 56% in counties where in-person classes were taking place, as compared to an overall decline of 17.9% where remote learning predominated. This data highlights the importance of academic institutions to reevaluate their COVID-19 mitigation policies as the pandemic continues.

BIOAEROSOL SAMPLING FOR SARS-COV-2 IN A REFERRAL CENTER WITH CRITICALLY ILL COVID-19 PATIENTS MARCH-MAY 2020

Lane MA, Brownsword EA, Babiker A, Ingersoll JM, Waggoner J, Ayers M, Klopman M, Uyeki TM, Lindsley WG, Kraft CS..
Clin Infect Dis. 2021 Jan 28:ciaa1880. doi: 10.1093/cid/ciaa1880. Online ahead of print.
Level of Evidence: 5 - Mechanism-based reasoning

BLUF

Researchers from Emory University in conjunction with the CDC investigated the extent of aerosolized SARS-CoV-2 particles, by using 8 National Institute for Occupational Safety and Health (NIOSH) BC 251 two-stage cyclone samples in six units throughout a tertiary care hospital in Atlanta, Georgia from March - May 2020. They collected a total of 528 aerosolized samples from medical units, ICUs, inpatient hallways, nursing stations and visitor corridors, all of which were negative by rRT-PCR for SARS-CoV-2. The authors note their promising results suggest a decreased likelihood of transmission as compared to previously thought, however, they acknowledge there is still much to be learned about COVID-19, and every precautionary step should continue to be taken to decrease exposure of health care personnel.

ABSTRACT

BACKGROUND: Previous research has shown that rooms of patients with COVID-19 present the potential for healthcare-associated transmission through aerosols containing SARS-CoV-2. However, data on the presence of these aerosols outside of patient rooms are limited. We investigated whether virus-containing aerosols were present in nursing stations and patient room hallways in a referral center with critically ill COVID-19 patients. METHODS: Eight National Institute for Occupational Safety and Health BC 251 two-stage cyclone samplers were set up throughout six units, including nursing stations and visitor corridors in intensive care units and general medical units, for six hours each sampling period. Samplers were placed on tripods which held two samplers positioned 102 cm and 152 cm above the floor. Units were sampled for three days. Extracted samples underwent reverse transcription polymerase chain reaction for selected gene regions of the SARS-CoV-2 virus nucleocapsid and the housekeeping gene human RNase P as an internal control. RESULTS: The units sampled varied in the number of laboratory-confirmed COVID-19 patients present on the days of sampling. Some of the units included patient rooms under negative pressure, while most were maintained at a neutral pressure. Of 528 aerosol samples collected, none were positive for SARS-CoV-2 RNA by the estimated limit of detection of 8 viral copies/m 3 of air. CONCLUSION: Aerosolized SARS-CoV-2 outside of patient rooms was undetectable. While healthcare personnel should avoid unmasked close contact with each other, these findings may provide reassurance for the use of alternatives to tight-fitting respirators in areas outside of patient rooms during the current pandemic.

DEVELOPMENT AND VALIDATION OF A PREDICTION MODEL FOR TOCILIZUMAB FAILURE IN HOSPITALIZED PATIENTS WITH SARS-COV-2 INFECTION

Mussini C, Cozzi-Lepri A, Menozzi M, Meschiari M, Franceschini E, Milic J, Brugioni L, Pietrangelo A, Girardis M, Cossarizza A, Tonelli R, Clini E, Massari M, Bartoletti M, Ferrari A, Cattelan AM, Zuccalà P, Lichtner M, Rossotti R, Girardi E, Nicastri E, Puoti M, Antinori A, Viale P, Guaraldi G.. PLoS One. 2021 Feb 23;16(2):e0247275. doi: 10.1371/journal.pone.0247275. eCollection 2021.

Level of Evidence: 4 - Case-series, case-control studies, or historically controlled studies

BLUF

A secondary analysis of the Tocilizumab in Patients with Severe COVID-19 Pneumonia (TESEO) study conducted at the Azienda Ospedaliero-Universitaria, Policlinico of Modena during March-July, 2020 by the Department of Infectious Diseases found among 266 patients treated with tocilizumab, by 28 days, 40 (15%) patients either received mechanical ventilation or died. Elevated platelets and decreased C-reactive protein were highly associated with the 28-day outcome of mechanical ventilation or death (Table 1). These results were used to develop a proposed risk score (Table 4), which could be used to identify patients at risk of failing tocilizumab treatment and progressing to mechanical ventilation or death.

FIGURES

Table 4

Risk score for mechanical ventilation/death on tocilizumab: Exact and simplified risk score.

A)

Characteristic	Coefficient of logistic regression	Simplified individual score	Example for virtual participant			
			Observed characteristic	Contribution	Exact propensity score from model	Total Score
Gender						
Female	0	0				
Male	0.91	+4	X	+4		
CRP mg/dL Day 4						
0–1.24	0	0				
1.24+	0.99	+4	X	+4		
PaO_2/FiO_2 ratio mmHg						
210+	0	0	X	0		
0–209	1.74	+6				
Platelets/mm^3						
334+	0	0	X	0		
0–333	0.71	+3				
Total score				+8	12.4%	+8

A male with CRP above the median but PaO_2/FiO_2 ratio and platelets below the median, has an individual score of +8 which corresponds to an estimated propensity to fail tocilizumab of 12.4%

B) Propensity score relative to simplified score

Simplified Score category	Estimated propensity to fail tocilzumab
Low (0–4)	0–10%
Intermediate (5–9)	10–20%
High (10+)	20%+

C)

The exact formula to calculate the propensity score for a participant i)

PS(i) = Num(i) / Den(i)

Where

Num(i) = exp (-3.85+0.91*male+0.99*CRP+1.74*PaO2/FiO2 ratio +0.71*PLT)

Den(i) = 1 + exp (-3.85+0.91*male+0.99*CRP+1.74*PaO2/FiO2 ratio +0.71*PLT)

In the example of the virtual participant above:

Num(i) = exp (-3.85+0.91+0.99) = 0.0843; Den (i) = 1 + 0.0843; PS = 12.4%

https://doi.org/10.1371/journal.pone.0247275.t004

Table 1. Mean of biomarkers by case-control status.

	Case-Control status			
Markers	**Mech Ventilation-Death**	**Free of event**	**p-value***	**Total**
	N = 40	N = 226		N = 266
Markers, Mean (SD)				
Female, n(%)	5 (12.5%)	84 (37.2%)	0.002	89 (33.5%)
Age, years	69 (8)	63 (13)	0.005	64 (13)
SOFA Score	3 (2)	2 (1)	< .001	2 (1)
PaO_2/FiO_2 mmHg				
Baseline	193.6 (113.4)	241.5 (101.2)	0.010	234.2 (104.3)
Day 4	124.1 (79.3)	244.1 (108.0)	< .001	225.2 (112.7)
Day 9	152.9 (116.6)	247.1 (117.1)	0.002	231.1 (121.8)
Change from baseline at Day 4	-96.3 (106.0)	18.4 (98.7)	< .001	0.0 (108.1)
Change from baseline at Day 9	-77.5 (148.2)	23.6 (126.7)	0.005	7.1 (135.0)
Respiratory rate				
Baseline	25.3 (7.2)	21.7 (5.7)	0.002	22.2 (6.0)
Day 4	25.4 (5.5)	21.1 (7.8)	0.024	21.5 (7.7)
Day 9	23.3 (5.7)	19.9 (8.8)	0.182	20.3 (8.6)
Change from baseline at Day 4	2.4 (7.2)	-1.0 (9.4)	0.159	-0.6 (9.2)
Change from baseline at Day 9	0.8 (8.2)	-1.9 (10.0)	0.365	-1.5 (9.8)
IL-6, pg/ml				
Baseline	318.6 (210.4)	318.1 (430.8)	0.997	318.2 (410.2)
Day 4	2210 (282.6)	797.8 (726.2)	< .001	910.8 (799.2)
Day 9	1323 (1382)	686.6 (755.2)	0.262	713.6 (777.1)
Change from baseline at Day 4	1783 (399.5)	460.3 (693.1)	< .001	578.4 (770.2)
Change from baseline at Day 9	1181 (1525)	217.5 (880.1)	0.155	274.2 (922.5)
D-dimer, mg/dl				
Baseline	1121 (1647)	1323 (3346)	0.819	1302 (3213)
Day 4	3066 (7028)	2467 (4098)	0.670	2522 (4409)
Day 9	2649 (3615)	2423 (4128)	0.864	2453 (4043)
Change from baseline at Day 4	1485 (8159)	567.8 (4748)	0.594	658.6 (5134)
Change from baseline at Day 9	2295 (4710)	582.5 (6511)	0.534	745.6 (6351)
CRP, mg/dL				
Baseline	12.9 (7.7)	10.0 (7.6)	0.035	10.5 (7.7)
Day 4	5.4 (5.0)	3.2 (3.8)	0.005	3.6 (4.1)
Day 9	7.1 (11.5)	1.4 (3.2)	< .001	2.1 (5.5)
Change from baseline at Day 4	-7.3 (8.9)	-6.8 (8.7)	0.759	-6.9 (8.7)
Change from baseline at Day 9	-4.6 (14.8)	-8.8 (8.6)	0.069	-8.2 (9.7)
Tot Lymphocytes, cells/mm^3				
Baseline	335.2 (616.7)	612.5 (947.4)	0.112	571.3 (910.1)
Day 4	642.6 (1321)	819.2 (1146)	0.441	792.7 (1172)
Day 9	1025 (1852)	1110 (1607)	0.816	1097 (1642)
Change from baseline at Day 4	78.3 (882.6)	62.3 (728.4)	0.919	64.6 (750.0)
Change from baseline at Day 9	-104 (561.6)	395.6 (1013)	0.033	324.2 (975.5)
Platelets, cells/mm^3				
Baseline	198.1 (97.7)	244.5 (111.5)	0.020	237.7 (110.6)
Day 4	236.9 (113.2)	337.0 (144.5)	< .001	322.3 (144.6)
Day 9	210.8 (92.7)	348.0 (141.8)	< .001	328.5 (143.9)
Change from baseline at Day 4	31.4 (82.3)	92.7 (98.9)	0.001	83.6 (98.9)

(*Continued*)

Table 1. (Continued)

	Case-Control status			
Markers	**Mech Ventilation-Death**	**Free of event**	**p-value***	**Total**
Change from baseline at Day 9	0.4 (104.0)	119.7 (127.3)	< .001	104.0 (130.6)

*Chi2 for gender and unpaired t-test

IDIOPATHIC IPSILATERAL EXTERNAL JUGULAR VEIN THROMBOPHLEIBITIS AFTER CORONAVIRUS DISEASE (COVID-19) VACCINATION

Martínez EL.. AJR Am J Roentgenol. 2021 Feb 24. doi: 10.2214/AJR.21.25708. Online ahead of print.
Level of Evidence: 5 - Case Report

BLUF

A physician from Doctor Peset University Hospital in Valencia, Spain details a case of a 55-year-old female developing unprovoked thrombophlebitis 2 weeks post second injection of Pfizer-BioNTech COVID-19 vaccination in her ipsilateral external jugular vein (Figure 1). Subsequent hyper-coagulability workup was negative, suggesting a possible association. However, the author admits that this case of thrombophlebitis may be coincidental given that over 180 million COVID-19 vaccinations have been administered world-wide without correlation, and that this case should not alter vaccine recommendations.

FIGURES

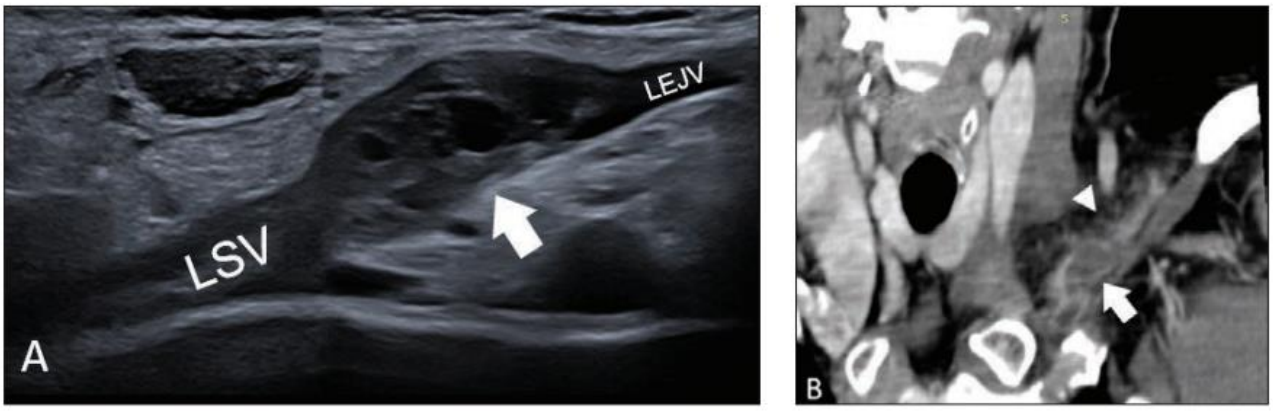

Figure 1. 55-year-old woman with left supraclavicular lump. Transverse panoramic ultrasound of the left supraclavicular region (A) and coronal oblique contrast-enhanced CT (B) show thrombus (arrow) in left external jugular vein extending to the left subclavian vein, with adjacent fat stranding (arrowhead), consistent with acute thrombophlebitis. LSV = left subclavian vein, LEJV = left external jugular vein.

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