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Upper Extremity Vascular Complications and COVID

2022 Florida Vascular Society Scientific Sessions

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Conflicts of Interest:

None.

Background

- For the past couple of years, we have been dealing with the novel coronavirus that caused a pandemic.
- As it mainly manifests as a respiratory illness, we have dealt with the non-respiratory consequences as well.
- In regards to vascular surgery, we have been dealing with coagulopathy-related complications, in the form of venous and arterial thromboembolism.
- Although arterial complications are less frequent than venous, it have proven to be a significant contributor to mortality and morbidity of COVID-19 patients.

Centers of Disease Control and Prevention. COVID-19 Weekly Cases and Death per 100,000 Population by Age, Race/Ethnicity, and Sex COVID Data Tracker2021 [cited 2022 January]. Available from: https://covid.cdc.gov/covid-data-tracker/#demographicsovertime.

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Case Presentation

Acute upper limb ischemia as the first manifestation in a patient with COVID-19

Tony Shao, MD, Christina In Bok Lee, BS, Sinan Jabori, BS, Jorge Rey, MD, Elizabeth Ramos Duran, MD, *and* Naixin Kang, MD, *Miami, Fla*

71 year old man presented with the chief complaint of severe pain / weakness of his arm and hand for 3 days.

ROS: +cough and dyspnea for more than 10 days

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Vitals:

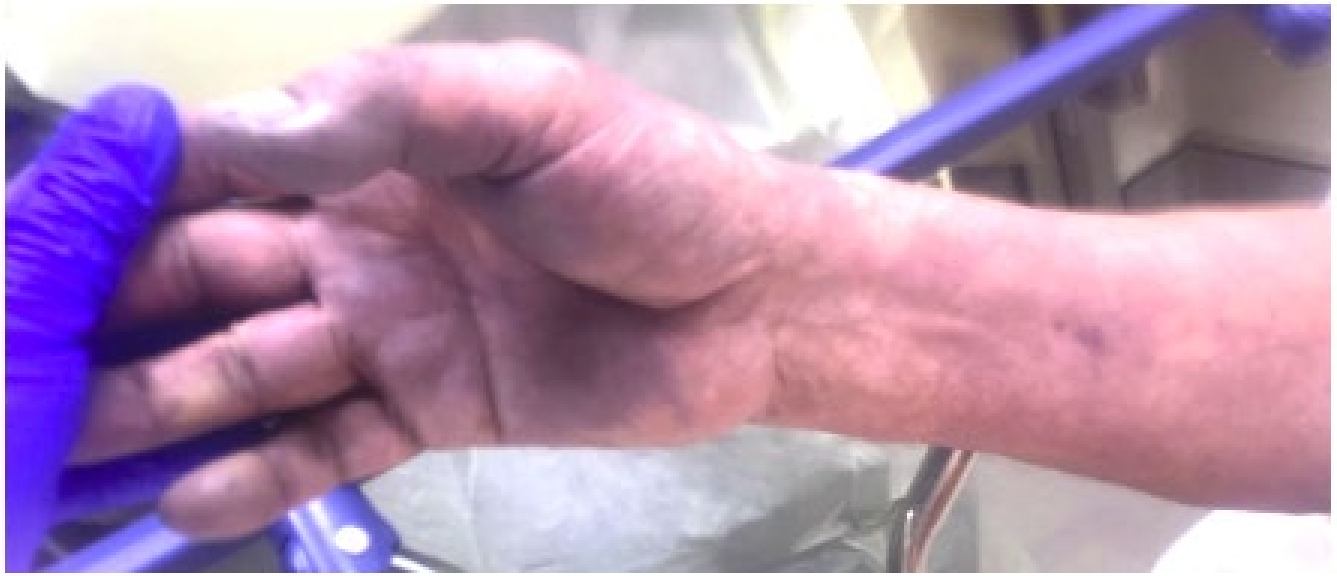
BP: 143/74 mmHg

HR: 97

RR: 20

Temp: 37.7 C

O2 sat: 88 on RA



PE:

NAD

Coarse crackles on bilateral lung bases

Pround ischemic changes of the hand and forearm with motor and sensory deficits

Palpable axillary pulse, no brachial and distal pulses

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Laboratory

Labs	Values
Hemoglobin	15.2 g/dL (12–15.5 g/dL),
total leucocyte count	8.6 x 10^3 /µL (4.5–11 x 10^3 /µL),
absolute neutrophil count	7.1 x 10^3 /µL (1.7–7 x 10^3 /µL)
absolute lymphocyte count	0.9 x 10^3 /µL (0.9–2.9 x 10^3 /µL)
platelets	331 x 10^3 /µL (140–440 x 10^3 /µL)
BUN	30 mg/dL (8.6– 10.3 mg/dL)
Serum Cr	1.45 mg/dL (0.60–1.30 mg/ dL)
Troponin	0.046 ng/mL (<0.03 ng/mL)
PT	12.1 s (9.9–13 s)
INR	0.9 (0.9– 1.1)
PTT	29.8 s (25.2–37.4 s)
D-dimer	1.85 mcg/mL (0.50 mcg/mL)

Labs	Values
lactate dehydrogenase	2010 U/L (140–271 U/L)
CRP	111.9 mg/L (9.9 mg/L)
ferritin level	1137 ng/mL (16.4– 294 ng/mL)
CK	>100,000 U/L (30–223 U/L)
lactic acid	1.7 mmol/L (0.5–2.2 mmol/L)

Blood gas analysis showed hypoxemia and respiratory alkalosis
Nasopharyngeal swab for COVID 19: **positive**

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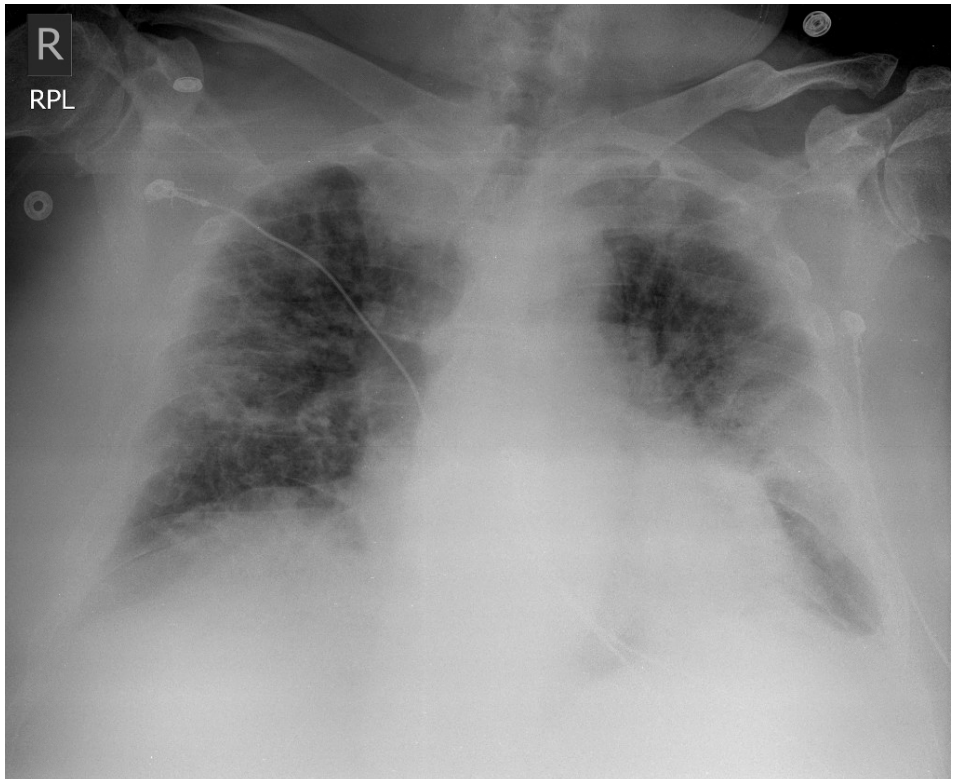

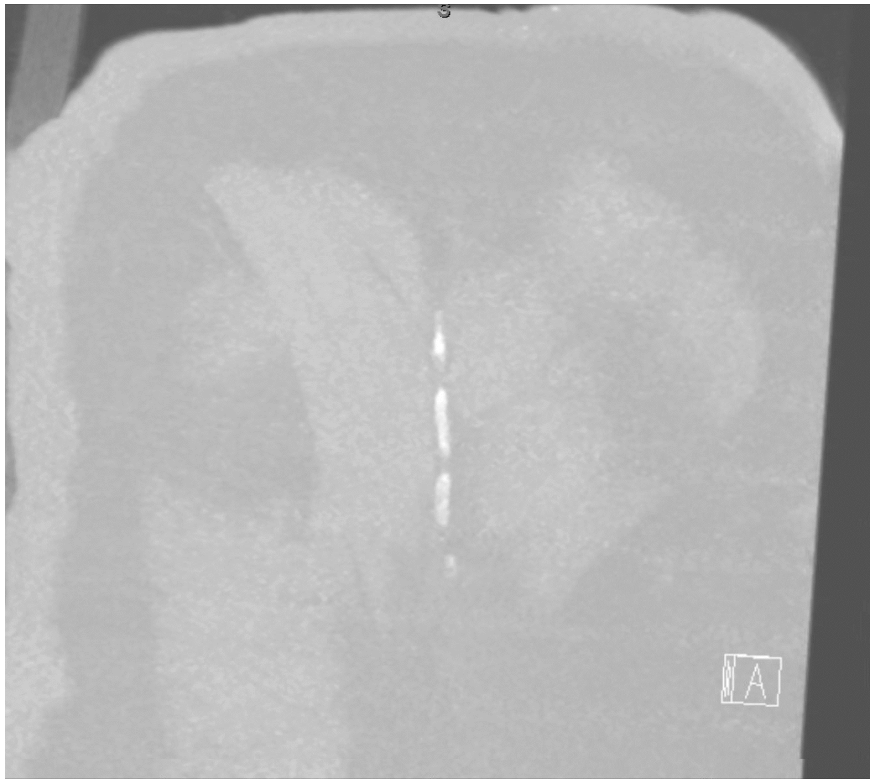

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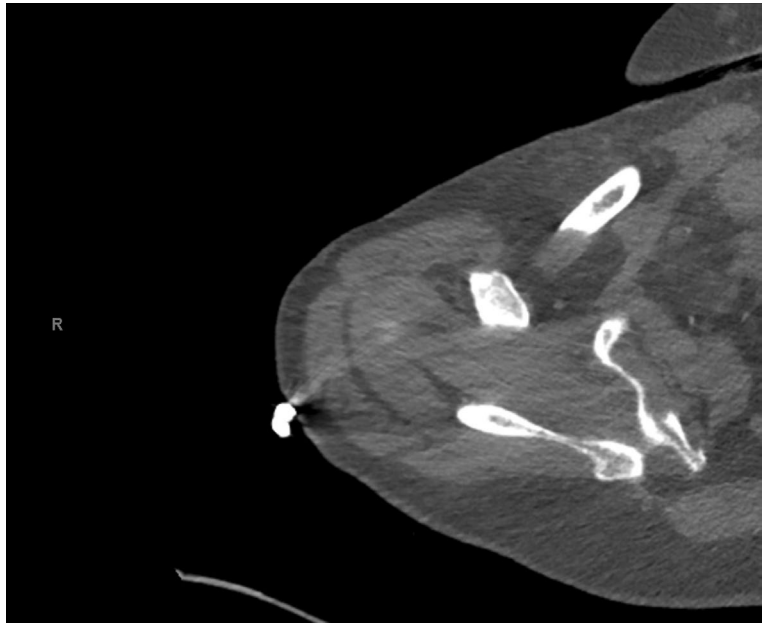

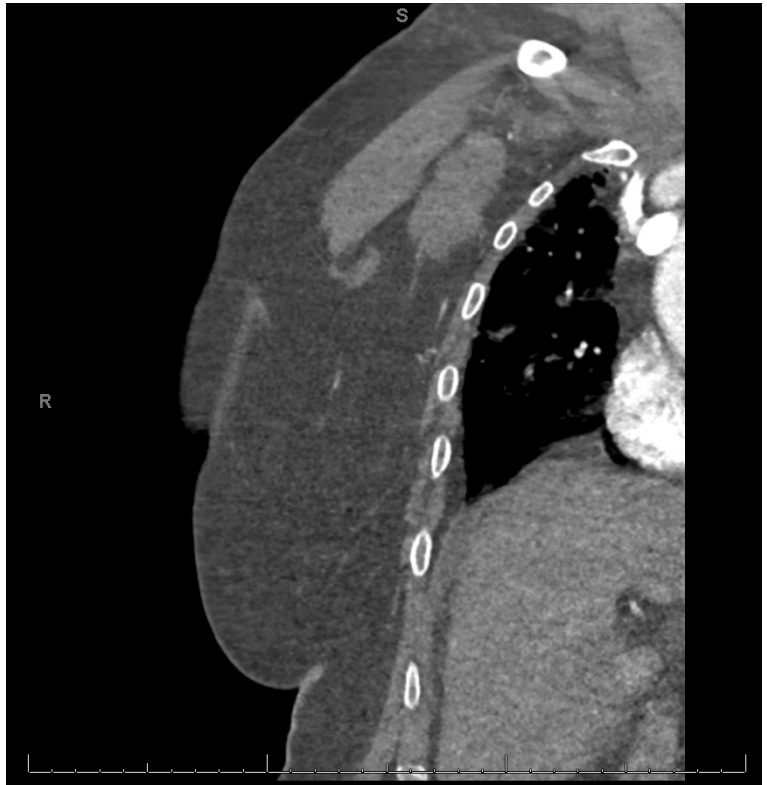

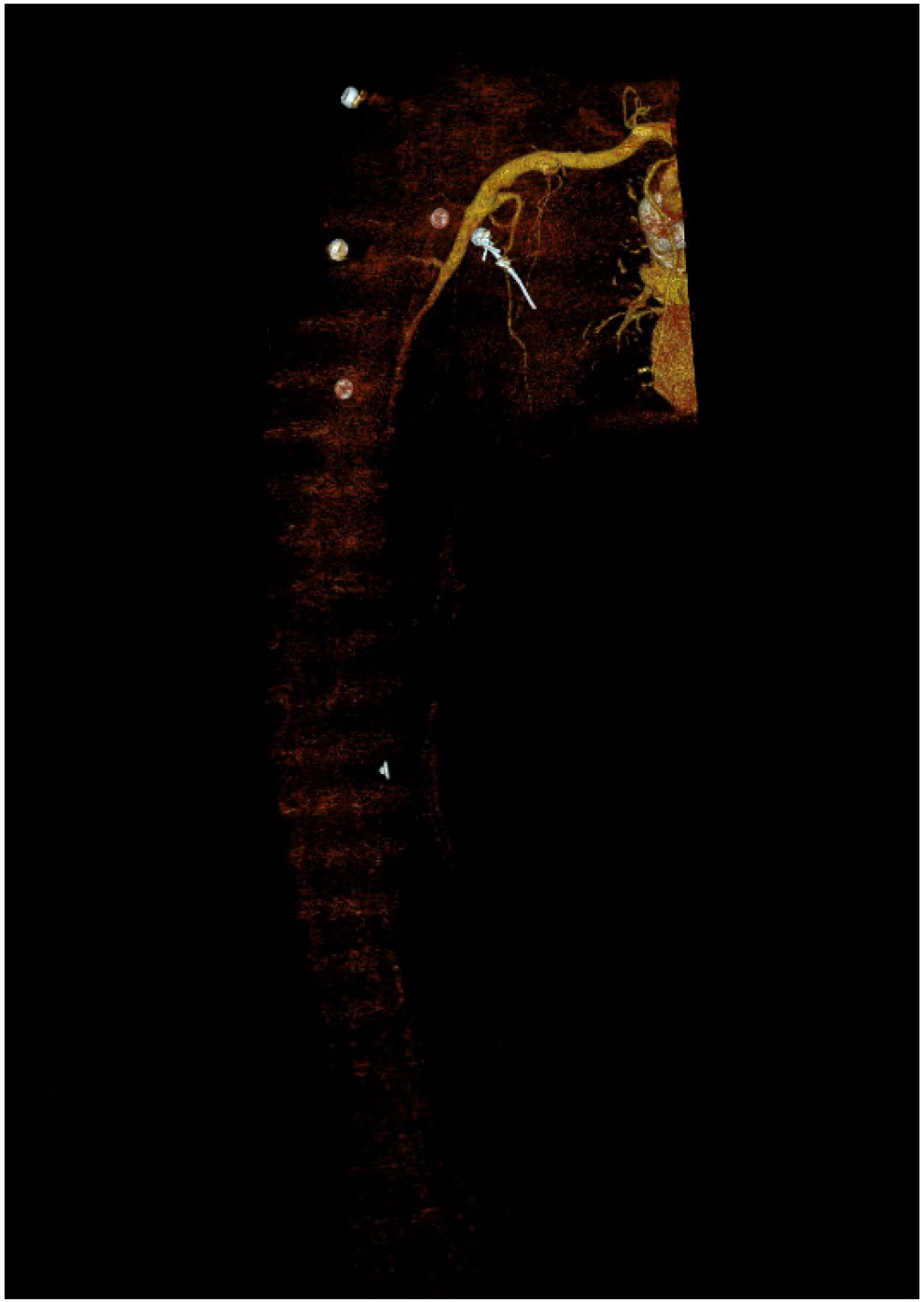

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Surgery

Open embolectomy of the brachial, radial, ulnar arteries via arm incisions

Forearm and hand fasciotomies

General anesthesia

EBL 100 cc

Hospital course

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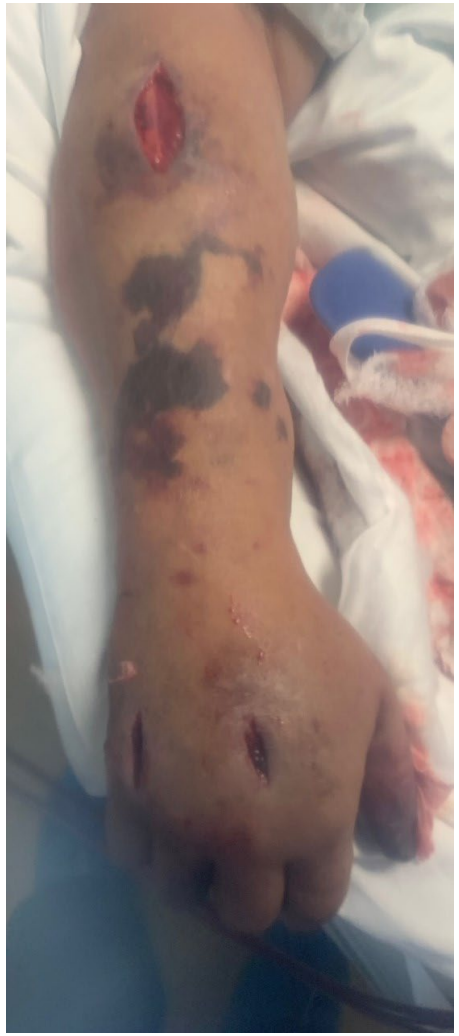
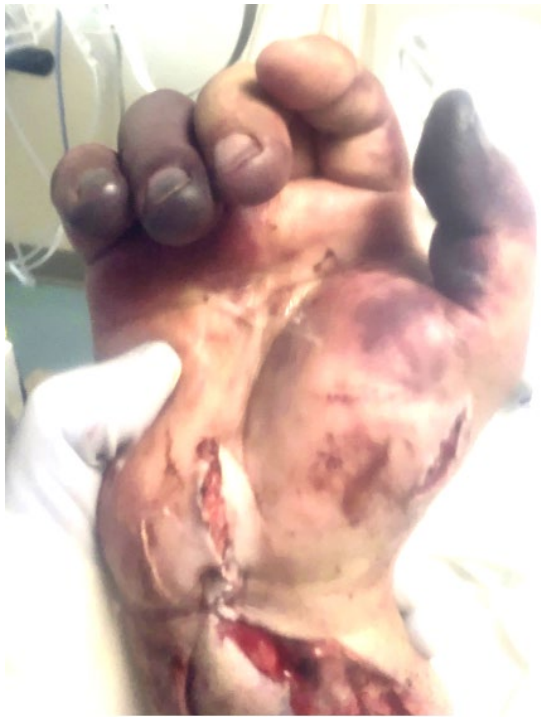
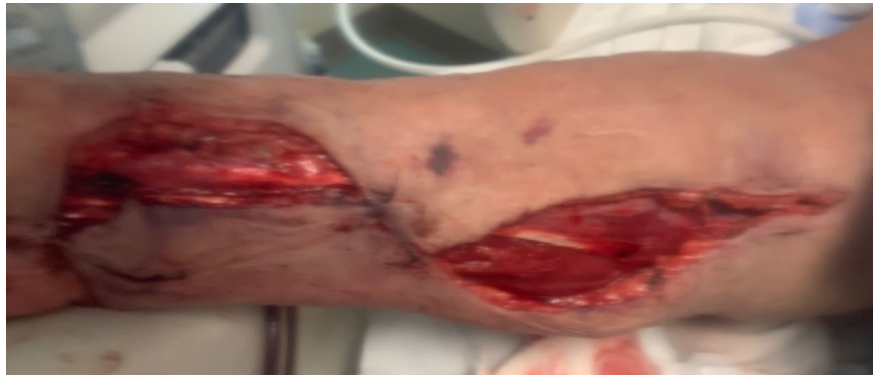


Radial and ulnar pulses were restored
Forearm muscles were grossly viable
Fingers demarcating
Persistent weakness of the hand





COVID-19 Related Thrombotic Complications Experience Before and During Delta Wave

Thrombotic events

	non-Delta n=206	Delta n=50	P-value
Venous Thrombosis – N (%)	155 (75%)	41 (82%)	0.31
Arterial Thrombosis – N (%)	85 (41%)	18 (36%)	0.50
Location – N (%)			
Upper extremity	43 (21%)	11 (22%)	0.86
Lower extremity	131 (63%)	33 (66%)	0.75
PE	58 (28%)	14 (28%)	0.98
MI	12 (6%)	2 (4%)	0.61
Aortic thrombus	3 (1%)	1 (2%)	0.78
Stroke	3 (1%)	0 (0%)	0.39
Multiple Thrombotic Locations*	74 (36%)	16 (32%)	0.60
Time of Thrombosis – in days* [IQR]	5 [1-11]	2 [1-13]	0.92
Anticoagulation treatment – N (%)	185 (90%)	44 (88%)	0.71
Start of anticoagulation – in days [IQR]**	2 [1-10]	1 [1-5]	0.22
DVT prophylaxis – N (%)	133 (64%)	25 (50%)	0.057
Surgery – N (%)	25 (12%)	5 (10%)	0.67
ICU – N (%)	157 (76%)	38 (76%)	0.97
Deceased – N (%)	78 (38%)	21 (42%)	0.61
D-dimer – in [IQR]	9 [3-2]	6 [3-13]	0.16
Fibrinogen – in [IQR]	384 [280-546]	355[150-518]	0.29
PT – in [IQR]	15 [15-17]	16 [15-18]	0.33
aPTT – in [IQR]	37 [30 – 59]	50 [35-87]	0.008
Ferritin – in [IQR]	794[412-1,365]	861[327-1,892]	0.72

(*)Time of thrombosis detection in days since hospital admission.
(**) Start of anticoagulation treatment in days since hospital admission.

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Effectiveness of therapeutic heparin versus prophylactic heparin on death, mechanical ventilation, or intensive care unit admission in moderately ill patients with covid-19 admitted to hospital: RAPID randomized clinical trial

Sholzberg, M., Tang, G. H., Rahhal, H et al.

- **Background:** Randomized trials suggest therapeutic heparin is beneficial in moderately ill COVID-19 patients

- **Objective:** To evaluate the effects of therapeutic heparin compared with prophylactic heparin among moderately ill patients with Covid-19 admitted to hospital wards.

- **Methods:** Open label randomised controlled trial conducted at 28 hospitals in six countries.

- **Primary outcome measured:** a composite of death, invasive and non-invasive mechanical ventilation, or admission to an ICU

RAPID randomized clinical trial (cont.)

Sholzberg, M., Tang, G. H., Rahhal, H et al.

Results:

- The primary outcome had occurred in 37/228 patients (16.2%) assigned to therapeutic heparin vs 52/237 (21.9%) assigned to prophylactic heparin
  - (odds ratio 0.69, 95% CI [0.43 to 1.10]; **P=0.12**)
- Deaths occurred in 4 patients (1.8%) assigned to therapeutic heparin vs 18 patients (7.6%) assigned to prophylactic heparin
  - (odds ratio 0.22, 95% CI [0.07 to 0.65]; **P=0.006**)

Conclusions:

- Therapeutic heparin was not significantly associated with a reduction in the primary outcome (a composite of death, invasive and non-invasive mechanical ventilation, or admission to an ICU)
  - but was associated with reduced odds of death at 28 days in moderately ill patients with Covid-19

Efficacy and Safety of Therapeutic-Dose Heparin vs Standard Prophylactic or Intermediate-Dose Heparins for Thromboprophylaxis in High-risk Hospitalized Patients With COVID-19: The HEP-COVID Randomized Clinical Trial

Alex C. Spyropoulos, Mark Goldin, Dimitrios Giannis et al.

- **Background:** Optimal thromboprophylaxis dosing in high-risk COVID patients is unknown.

- **Objective**: To evaluate the effects of therapeutic-dose LMWH vs institutional standard prophylactic or intermediate-dose heparins for thromboprophylaxis in high-risk hospitalized patients with COVID-19.

- **Methods:** multicenter randomized clinical trial recruited hospitalized adult patients with COVID-19 with 4x elevated D-dimer levels or sepsis-induced coagulopathy score from May 8,2020, through May 14, 2021

- **Primary outcome measured:** venous thromboembolism (VTE), arterial thromboembolism (ATE), or death from any cause

The HEP-COVID Randomized Clinical Trial (cont.)

Results:

- Decreased venous thromboembolism (VTE), arterial thromboembolism (ATE), or death from any cause when comparing therapeutic-dose LMWH to standard-dose heparin (RR 0.68; 95% CI, 0.49-0.96; **P= .03**)
  - Standard-dose heparin: 41.9% had VTE, ATE, or death from any cause
  - LMWH heparin: 28.7 had VTE, ATE, or death from any cause
- The incidence of major bleeding was 1.6% with standard-dose heparin vs 4.7% with therapeutic-dose heparins (RR 2.88; 95% [CI 0.59-14.02] P= .17).
- The primary efficacy outcome was reduced in non-ICU patients but not ICU patients (36.1% vs 16.7%) (RR: 0.46 [95% CI 0.27-0.81] **P= .004**)

Conclusion:

- Therapeutic-dose LMWH reduced major thromboembolism and death compared with institutional standard heparin thromboprophylaxis among inpatients with COVID-19 with very elevated D-dimer levels

Table 2. Clinical Outcomes During the 30-Day Postrandomization Phase

Outcome	No./total No. (%)		RR (95% CI)	*P* value[a]
	Therapeutic dose (n = 129)	Standard dose (n = 124)		
Primary efficacy outcome				
VTE, ATE, or death	37/129 (28.7)	52/124 (41.9)	0.68 (0.49-0.96)	.03
Non-ICU stratum	14/84 (16.7)	31/86 (36.1)	0.46 (0.27-0.81)	.004
ICU stratum	23/45 (51.1)	21/38 (55.3)	0.92 (0.62-1.39)	.71
VTE + ATE	14/129 (10.9)	36/124 (29.0)	0.37 (0.21-0.66)	<.001
Death	25/129 (19.4)	31/124 (25.0)	0.78 (0.49-1.23)	.28

Therapeutic versus prophylactic anticoagulation for patients admitted to hospital with COVID-19 and elevated D-dimer concentration (ACTION): an open-label, multicentre, randomised, controlled trial

Renato L, Pedro S., Remo F. et al.

- **Objective**: aimed to compare the efficacy and safety of therapeutic versus prophylactic anticoagulation in this population

- **Methods:** open-label, multicentre, randomised, controlled trial at 31 sites in Brazil.
  - Therapeutic anticoagulation:
    - Oral rivaroxaban (15-20 mg daily) for stable patients
    - or initial subcutaneous enoxaparin (1 mg/kg twice per day) or IV unfractionated heparin followed by rivaroxaban to day 30 for clinically unstable patients
  - Prophylactic anticoagulation was standard in-hospital enoxaparin or unfractionated heparin.

- **Primary efficacy outcome measured:** time to death, duration of hospitalisation, or duration of supplemental oxygen to day 30
- **Primary safety outcome measured**: major or clinically relevant non-major bleeding through 30 days.

ACTION Trial (cont.)

Results:
No difference in primary efficacy outcome between patients assigned therapeutic or prophylactic anticoagulation. (0.86 [95% CI 0.59–1.22], p=0.40)
However, increased major or clinically relevant non-major bleeding in 26 (8%) of therapeutic anticoagulation group vs 7 (2%) in prophylactic anticoagulation group (RR 3.64 [95% CI 1.61–8.27], **p=0.0010**)

Conclusion:
Therapeutic anticoagulation of oral rivaroxaban or enoxaparin followed by rivaroxaban did not improve clinical outcomes and increased bleeding compared with prophylactic anticoagulation.

The COVID-19 Treatment Guidelines on Anticoagulation in Hospitalized Patients With COVID-19

For Hospitalized, Nonpregnant Adults Who Require Low-Flow Oxygen and Are Not Receiving Intensive Care Unit Level of Care

- The Panel recommends using **therapeutic-dose heparin** for patients who have a D-dimer above the upper limit of normal (ULN), require low-flow oxygen, and have no increased bleeding risk (CIIa). LMWH is preferred over unfractionated heparin.
- Based on clinical trial exclusion criteria, contraindications for therapeutic anticoagulation for COVID-19 due to an increased bleeding risk are as follows: platelet count <50, hemoglobin <8, need for dual antiplatelet therapy, known bleeding within the last 30 days requiring an emergency room visit or hospitalization, known history of a bleeding disorder, or an inherited or active acquired bleeding disorder. In patients without a VTE who are started on therapeutic-dose heparin, treatment should continue for 14 days or until hospital discharge, whichever comes first.

For Hospitalized, Nonpregnant Adults Who Are Receiving Intensive Care Unit Level of Care (Including Patients Who Are Receiving High-Flow Oxygen)

- The Panel recommends using **prophylactic-dose heparin** as VTE prophylaxis unless a contraindication exists (AI).
- The Panel recommends **against** the use of intermediate-dose (e.g., enoxaparin 1 mg/kg daily) and therapeutic-dose anticoagulation for VTE prophylaxis, except in a clinical trial (BI).
- For patients who start on therapeutic-dose heparin while on low-flow oxygen due to COVID-19 and then transfer to the intensive care unit (ICU), the Panel recommends switching from therapeutic to prophylactic-dose heparin unless a VTE is confirmed (BIII).

References

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Thank you