

thus prone to measured and unmeasured bias.<sup>6</sup> In another analysis, the authors have themselves pointed out that unmeasured confounders rather than biological superiority may explain the survival advantage of MAG in non-randomized series.<sup>7</sup>

To conclude, RCTs have shown that while MAG is associated with a better revascularization rate, it is not associated with mortality benefit compared with SAG. Also, MAG is associated with higher sternal complications.

## Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Khalid Chagal, MD<sup>a</sup>

Saqib Masroor, MD<sup>b\*</sup>

Salik Nazir, MD<sup>a</sup>

Sadik Khuder, PhD<sup>c</sup>

Ehab Eltahawy, MD, MPH<sup>a1</sup>

<sup>a</sup> Department of Cardiovascular Medicine, University of Toledo Health Sciences, Toledo, Ohio

<sup>b</sup> Department of Cardiothoracic Surgery, University of Toledo Health Sciences, Toledo, Ohio

<sup>c</sup> Department of Statistics, University of Toledo

Health Sciences, Toledo, Ohio

<sup>1</sup> Senior author.

18 July 2020

1. Chagal K, Masroor S, Elzanaty A, Patel M, Mir T, Khan S, Nazir S, Soni R, Oostra C, Khuder S, Eltahawy E. Meta-analysis comparing multiple arterial grafts versus single arterial graft for coronary-artery bypass grafting. *Am J Cardiol* 2020;130:46–55.
2. Kurlansky P, Gaudino M. Multiple arterial grafting: a critical analysis. *Am J Cardiol* 2020;S0002-9149.
3. Thuijs DJ, Head SJ, Stone GW, Puskas JD, Taggart DP, Serruys PW, Dressler O, Crowley A, Brown WM III, Horkay F, Boonstra PW. Outcomes following surgical revascularization with single versus bilateral internal thoracic arterial grafts in patients with left main coronary artery disease undergoing coronary artery bypass grafting: insights from the EXCEL trial. *Eur J Cardiothorac Surg* 2019;55:501–510.
4. Kolte D, Vlahakes GJ, Palacios IF, Sakhujia R, Passeri JJ, Inglessis I, Elmariah S. Transcatheter versus surgical aortic valve replacement in low-risk patients. *J Am Coll Cardiol* 2019;74:1532–1540.
5. Taggart DP, Benedetto U, Gerry S, Altman DG, Gray AM, Lees B, Gaudino M, Zamvar V, Bochenek A, Buxton B, Choong C. Bilateral versus single internal-thoracic-artery grafts at 10 years. *N Engl J Med* 2019;380:437–446.
6. Taggart DP, Gaudino MF, Gerry S, Gray A, Lees B, Dimagli A, Puskas JD, Zamvar V,

Pawlaczyk R, Roysse AG, Flather M, Benedetto U, ART investigators ART investigators. Effect of total arterial grafting in the Arterial Revascularization Trial. *J Thorac Cardiovasc Surg* 2020. <https://doi.org/10.1016/j.jtcvs.2020.03.013>. S0022-5223(20)3091-2.

7. Gaudino M, Di Franco A, Rahouma M, Tam DY, Iannaccone M, Deb S, D'Ascenzo F, Abouarab AA, Girardi LN, Taggart DP, Fremes SE. Unmeasured confounders in observational studies comparing bilateral versus single internal thoracic artery for coronary artery bypass grafting: a meta-analysis. *J Am Heart Assoc* 2018;7:e008010.

<https://doi.org/10.1016/j.amjcard.2020.07.055>

## Extensive Arterial Thrombosis in Covid-19



A 70-year-old woman with hypertension and type 2 diabetes presented to the hospital with a cold, pulseless, and pale left leg. On examination, her left leg was found to have mottling and pallor to the level of the proximal left calf. There were absent left femoral, popliteal, or pedal pulses. In contrast, there were palpable pedal pulses on the right side.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) reverse transcription polymerase chain reaction was positive. Computed tomography

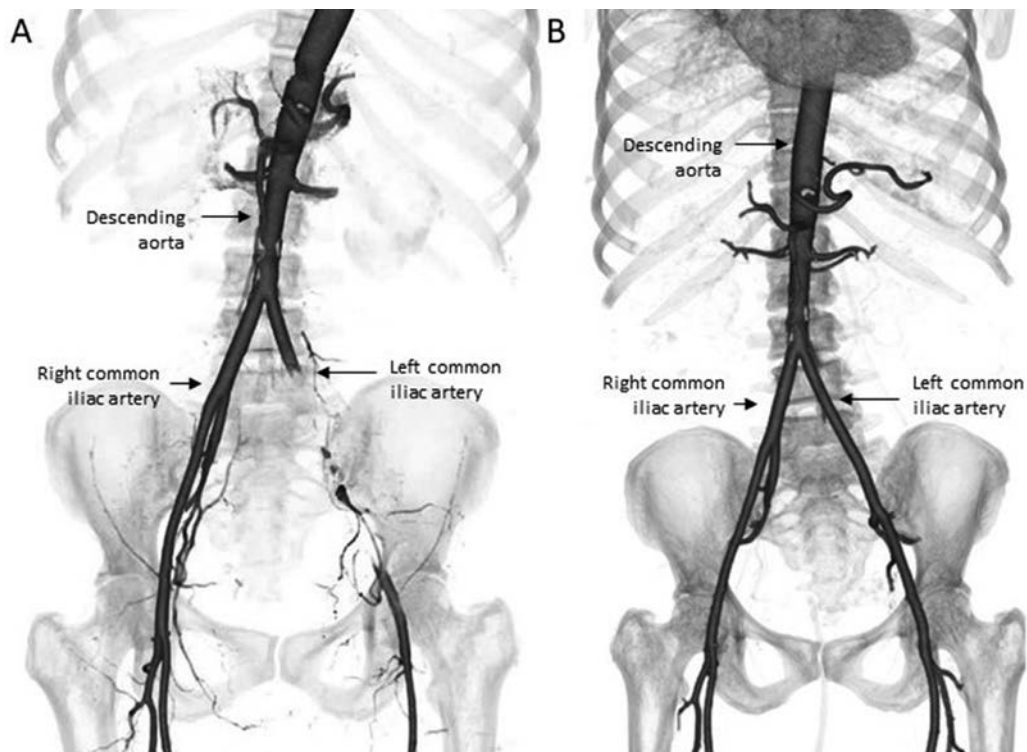


Figure 1. Computed tomography angiogram at initial presentation (left panel) and after emergent thrombectomy and thrombolysis (right panel). Consent for publication was obtained from the patient.

Table 1  
Laboratory findings on admission

	Laboratory results on admission	Reference range*
Platelet count (K/L)	217	150-450
D-dimer (ng/mL)	>4000	<500
Prothrombin time (sec)	14.6	11.5-14.5
International normalized ratio	1.2	0.9-1.1
Activated partial-thromboplastin time (sec)	26.6	23.8-36.6
Fibrinogen (mg/dL)	320	200-450
Lactate dehydrogenase (U/L)	642	135-225
Ferritin (ug/L)	617	13-150
High-sensitivity C-reactive protein (mg/L)	95	0-10
B2 glycoprotein 1 Ab, IgG (CU)	<6.4	0-19
B2 glycoprotein 1 Ab, IgM (CU)	12	0-19
Cardiolipin Ab, IgG (CU)	3	0-19
Cardiolipin Ab, IgM (CU)	53	0-19
Protein C Resistance	4.2	>2.2
Dilute Russell's viper venom time	Positive	Negative
Lupus anticoagulant (hexagonal phase)	Positive	Negative

\* Reference values are affected by many variables, including the patient population and the laboratory methods used. The ranges used at Brigham and Women's Hospital are for adults who are not pregnant and do not have medical conditions that could affect the results. They may therefore not be appropriate for all patients.

angiogram revealed extensive arterial thromboses including nonocclusive thrombus of the infrarenal abdominal aorta near the aortic bifurcation, occlusion of the left common iliac artery, internal iliac artery, and external iliac artery to the level of the iliac ligament with complete occlusion of the popliteal artery below the knee and its branches (Figure 1, left panel). The patient had no history of venous or arterial clots, no known vasculopathy, minimal underlying atherosclerosis, no personal or family history of hypercoagulable disease, no aortic compression as nidus for thrombus formation, and evaluation for malignancy has been negative to date. An initial hypercoagulable workup (Table 1) found a positive lupus anticoagulant by dilute Russell's viper venom time and hexagonal phase assays.

Hypercoagulability and endothelial injury have been described as features of coronavirus disease 2019 (Covid-19). While asymptomatic or symptomatic venous thromboembolism has been frequently observed, arterial thrombosis and acute limb ischemia have less commonly been described.<sup>1</sup> Lupus anticoagulant has been identified commonly in Covid-19,<sup>2</sup> and if persistent, is known to be associated with thrombosis in antiphospholipid syndrome. In this case, lupus anticoagulant may have been a false-positive test result in context of acute illness and the receipt of unfractionated heparin. Critical illness and

marked inflammatory response in the setting of Covid-19 likely increased propensity for thrombus formation and acute limb ischemia in this patient.

She underwent emergent thrombectomy and thrombolysis and 4-compartment fasciotomy, with limb salvage and revascularization (Figure 1, right panel). She was initially treated with unfractionated heparin and was bridged to warfarin for maintenance anticoagulation, and discharged to rehabilitation for ongoing recovery. Heightened clinical vigilance is needed for early identification of this potentially serious complication of Covid-19 to facilitate prompt intervention targeting limb salvage.<sup>3-6</sup> Further research is needed to determine the role of hypercoagulability in Covid-19, and to identify strategies to prevent and treat venous and arterial thrombosis in this setting.

### Disclosures

Dr Vaduganathan is supported by the KL2/Catalyst Medical Research Investigator Training award from Harvard Catalyst (NIH/NCATS Award UL1TR002541), serves on advisory boards for Amgen, AstraZeneca, Baxter Healthcare, Bayer AG, Boehringer Ingelheim, Cytokinetics, and Relypsa, and participates on clinical endpoint committees for studies sponsored by Novartis and the NIH. All other authors report no disclosures.

Lauren E. Merz, MD, MSc

Lauren Sinnenberg, MD

Marie D. Gerhard-Herman, MD

Muthiah Vaduganathan, MD, MPH\*

Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts  
21 July 2020

1. Bellosa R, Luzzani L, Natalini G, Pegorer MA, Attisani L, Cossu LG, Ferrandina C, Fos-sati A, Conti E, Bush RL, Piffaretti G. Acute limb ischemia in patients with COVID-19 pneumonia. *J Vasc Surg* 2020.
2. Bowles L, Plotton S, Yartey N, Dave M, Lee K, Hart DP, MacDonald V, Green L, Sivapalaratnam S, Pasi KJ, MacCallum P. Lupus anti-coagulant and abnormal coagulation tests in patients with Covid-19. *N Engl J Med* 2020;383:288-290.
3. National Institutes of Health. COVID-19 treatment guidelines panel coronavirus disease-2019 (COVID-19) treatment guidelines. Available at: <https://www.covid19-treatmentguidelines.nih.gov/>. Accessed June 4, 2020.
4. Gerhard-Herman MD, Gornik HL, Barrett C, Barshes NR, Corriere MA, Drachman DE, Fleisher LA, Fowkes LGR, Hamburg NM, Kinlay S, Lookstein R, Misra S, Mureebe L, Olin JW, Patel RA, Regensteiner JG, Schanzer A, Shishchbor MH, Stewart KJ, Treat-Jacobson D, Walsh ME. 2016 AHA/ACC guideline on the management of patients with lower extremity peripheral artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2017;69:1465-1508.
5. Thachil J, Tang N, Gando S, Falanga A, Cattaneo M, Levi M, Clark C, Iba T. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *J Thromb Haemost* 2020;18:1023-1026.
6. Connors JM, Levy JH. Thromboinflammation and the hypercoagulability of COVID-19. *J Thromb Haemost* 2020;18:1559-1561.  
<https://doi.org/10.1016/j.amjcard.2020.07.056>

### Meta-analysis Assessing the Effect of Sodium-Glucose Co-transporter-2 Inhibitors on Left Ventricular Mass in Patients With Type 2 Diabetes Mellitus



Type 2 diabetes mellitus (T2DM) has evolved as a pandemic of the 21st century, while cardiovascular disease (CVD) affects almost one third of patients and represents the cause of death

Conflicts of interests: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.