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Incertitude Pathophysiology and Management During the First Phase of the COVID-19 Pandemic



TO THE EDITOR: The case report described by Fukuhara and colleagues¹ renders some considerations. First, the variability of the host immune response plays a crucial role in coronavirus disease 2019 (COVID-19) severity. During the COVID-19 illness, CD3⁺, CD4⁺, and CD8⁺ lymphocyte counts are reduced based on disease stage,² while the cytokine storm heralds adverse outcomes, which occur in patients with severe disease due to tumor necrosis factor- α and interleukins (IL) such as IL-6, IL-8, and IL-10.^{2,3} We recently reported that proinflammatory cytokines IL-6, IL-8, and tumor necrosis factor- α reach maximum levels 2 to 4 hours after cardiopulmonary bypass (CPB) and decrease to nearly normal levels within 24 hours.

Nonetheless, CPB, by interfering with coagulation, favors the expression of G protein-coupled receptors, which cause platelet and leukocyte activation. Factor Xa induces the expression of cytokines and adhesion molecules in leukocytes. Hence, coagulation is linked to inflammation. We also found that the proinflammatory cytokine burden correlates with worse postoperative outcomes.⁴ The patient described by the authors had a proinflammatory CPB response synergistically worsened by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.

Second, it is important to note that in countries affected by the pandemic during the initial phase of the propagation of SARS-CoV2 infection, no advisory committee for hospitalization practices had issued recommendations that identified guidelines for the prevention of COVID-19 in patients in which hospitalization was necessary. This vacancy in the predefined guidelines raised doubts about the timing in which patients acquired the COVID-19 disease, favoring the suspicion that the infection had occurred in the preoperative period, which was therefore not negligible.

For many patients who were hospitalized in critical condition requiring an immediate surgical procedure, SARS-CoV-2 was sometimes not even considered at presentation. The dysfunction was evident not only in smaller hospitals but also in tertiary referral centers. Many were limited by the number of available real-time polymerase chain reaction tests, and the relatively long processing times were not conducive to emergency interventions.

Finally, although we are better equipped to deal with SARS-CoV-2, some aspects linked to diagnostic management remain uncertain. Viral and serologic testing for acute SARS-CoV-2 infection is now recommended for surgical decision making. Nevertheless, there remains a

concern in patients with mild SARS-CoV-2 infection or asymptomatic patients who require emergency interventions but remain undetected by current screening procedures.

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REFERENCES

1. Fukuhara S, Rosati CM, El-Dalati S. Acute type A aortic dissection during the COVID-19 outbreak. *Ann Thorac Surg.* 2020;110:e405-e407.
2. Zhang X, Tan Y, Ling Y, et al. Viral and host factors related to the clinical outcome of COVID-19. *Nature.* 2020;583:437-440.
3. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet.* 2020;395:497-506.
4. Giacinto O, Satriano U, Nenna A, et al. Inflammatory response and endothelial dysfunction following cardiopulmonary bypass: pathophysiology and pharmacological targets. *Recent Pat Inflamm Allergy Drug Discov.* 2019;13:158-173.

COVID-19 and Cardiac Surgery: Still Many Questions and Much Work to Do



REPLY TO THE EDITOR: Dr Nappi¹ provides insightful comments and suggestions regarding the pathophysiology of coronavirus disease 2019 (COVID-19) and its likely compounding inflammatory effects with cardiopulmonary bypass on our patient's surgical outcome,² which we previously discussed in response to Manenti and colleagues.³ During the 10 weeks since our reply, the status of the pandemic has evolved. In the United States, while the total number of deaths has now surpassed half a million, the daily number of new cases and deaths has decreased dramatically, likely a reflection of the vaccination campaign that has begun here and despite fears of new viral variants.

Recently, new data have emerged about the impact of COVID-19 on cardiac surgery in the United States. During the 57th Annual Meeting of The Society of Thoracic Surgeons (STS), Nguyen and associates⁴ presented results of an analysis of The STS Adult Cardiac Surgery Database that showed a 53% decrease nationwide in the average monthly cardiac surgery volume compared with 2019, with 65% fewer elective and 40% fewer nonelective cases, regardless of procedure type. Not only is there a clear increased risk of morbidity and mortality with cardiac procedures during the pandemic,⁴ but our colleagues in New York have discovered that patients with COVID-19 requiring any kind of emergent surgical operation suffer greater perioperative morbidity and mortality overall.⁵ The current study by Nguyen and

colleagues has not yet elucidated specific reasons for increased mortality, and we look forward to learning from future data derived from such an extensive data set and commendable collaborative effort.

As we gain a better understanding how COVID-19 impacts patient outcomes for emergent procedures during this time, it will be crucial to develop guidelines to efficiently screen and identify patients with acute COVID-19 infection to mitigate the morbidity and mortality currently witnessed. It is of key importance that we continue working together to answer the many questions that remain and defeat the pandemic.

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REFERENCES

1. Nappi F. Incertitude pathophysiology and management during the first phase of the COVID-19 pandemic. *Ann Thorac Surg.* 2022;113:693.
2. Fukuhara S, Rosati CM, El-Dalati S. Acute type A aortic dissection during the COVID-19 outbreak. *Ann Thorac Surg.* 2020;110:e405-e407.
3. Rosati CM, Nguyen CTN, Fukuhara S. COVID-19 and aortic dissections: collaboration (among disciplines and centers) is key. *Ann Thorac Surg.* 2021;112:683.
4. Nguyen TC, Thourani VH, Nissen AP, et al. The effect of COVID-19 on adult cardiac surgery in the United States: analysis of The Society of Thoracic Surgeons Adult Cardiac Surgery Database. Presented at the 57th Annual Meeting of The Society of Thoracic Surgeons; virtual meeting, January 29-31, 2021.
5. Knisely A, Zhou ZN, Wu J, et al. Perioperative morbidity and mortality of patients with COVID-19 who undergo urgent and emergent surgical procedures. *Ann Surg.* 2021;273:34-40.

The Internal Thoracic Artery Remodeling



TO THE EDITOR: The interesting paper by Rodgers-Fischl and colleagues¹ concerns a particular contraindication to use the internal thoracic artery (ITA) as a conduit in coronary surgery, when this vessel works like an important collateral to revascularize the iliac-femoral district. In this case, ITA changes its main function from a “nutritional” artery, with many side-branches feeding thoracic wall structures and mediastinal organs, into a “conduit” vessel directing much of its flow to the superior epigastric artery, its straight extension. On selective angiography, this hemodynamics correlates with a delayed and poor opacification of ITA branches, reversely supplied by the intercostal arteries.¹ Differently, in case of aortic coarctation, the ITAs, important components of its secondary collateral network, work

reversing their blood flow, just since the birth and through the intercostal arteries, toward the descending thoracic aorta, in agreement with a pressure gradient. All this confirms the good plasticity of these vessels, embryologically developed from the primordial aortic arches, and correlates with the relevant elastic component of their walls. These characteristics allow ITAs to increase in size and flow, to supply an enlarged periphery, independently from its inflow pressure.^{2,3} On the contrary, the epigastric arteries, proper muscular vessels, maintain unchanged their size and “nutritional” function for the abdominal wall; however they cooperate to projects of collateral networks, typically in favor of the lower limbs, through their dense networks of branches, already present but progressively developed inside the abdominis recti muscles. This providential arrangement, in its organic feature, is promoted by different cell-signaling proteins, such as vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), transforming growth factor-beta (TGF- β), angiotensin-1 and 2, and, in its functional expression, by vasodilator mediators, all active mainly on medium/large sized elastic vessels.^{4,5} In conclusion, some features of a remodeled ITA can be explained on an anatomic-functional plane; in perspective, this methodology can be applied to better understand pathophysiology of other vascular collateral systems.

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REFERENCES

1. Rodgers-Fischl PM, Ferraris VA, Makdasi G. Is internal mammary to the anterior descending always the best option? *Ann Thorac Surg.* 2021;111:e425-e427.
2. Abreu JS, Tsutsui JM, Falcão SNR, et al. The impact of ligation of proximal side branches on blood flow and functional status of the internal thoracic artery in coronary anastomosis. *Echocardiography.* 2016;33:1656-1664.
3. Leloup AJA, Van Hove CE, Heykers A, et al. Elastic and muscular arteries differ in structure, basal NO production and voltage-gated Ca(2+)-channels. *Front Physiol.* 2015;6:375.