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Letter to the editor

Thrombocytopenia and coagulation disorders due to COVID 19 infection with concomitant cardiovascular diseases requiring anti-platelet and anticoagulant therapy, which strategy?

We read with a great interest the article published by Lippi and coworkers [1]. Our interest arises from a clinical case of our one patient who underwent on February 2020 complex cardiac surgery (Bentall-De Bono procedure associated with coronary artery grafting surgery), and who died on April 2020 for coronavirus disease, i.e. COVID 19, infection complicated by severe thrombocytopenia [2]. The patient took both antiplatelet aggregation therapy for ischemic heart disease and anticoagulant therapy for chronic atrial fibrillation. From this clinical case, we have focused the attention on the subgroup of patients affected by thrombocytopenia due to COVID-19 and concomitant cardiovascular diseases requiring antiplatelet aggregation and anticoagulant therapy. It should be emphasized that the studies making up the meta-analysis on this topic are very heterogeneous, and report different limits to define thrombocytopenia. Therefore, more detailed investigations are necessary in the future. It may be useful in these patients at the time of their admission a serum test, i.e. ROTEM or TEG, for the evaluation of platelet function [3]. In presence of severe COVID 19 disease, as well as of other coronaviruses, thrombocytopenia has been reported [4]. These tests can be useful to follow the progress of the disease and prevent and/or treat the different phases of the disseminated intravascular coagulopathy (DIC), resulting from a sum of vectors for hyper-coagulation or hyper-fibrinolysis state [5]. The virus invades host human cells by binding to the angiotensin converting enzyme 2 ACE-2 receptor. Coagulation disorders have been frequently detected among COVID 19 patients, especially those with severe forms: in fact, among many biomarkers involved in the development of DIC, several factors, i.e. D-Dimer, prothrombin time PT, activated partial thromboplastin time APTT, are altered. Moreover, it might be useful to consider the level of the von Willebrand factor. Patients with aortic stenosis or affected by bicuspid aortic valve disease often have an alteration of the von Willebrand factor. Are these patients more at risk of promoting a DIC, especially when a COVID 19 infection is present? Therefore, from the set of biomarkers deriving from pulmonary, coagulative and inflammatory alteration, it could be useful to create a score to differentiate the risk profile at the in-hospital admission, and to create specific therapeutic protocols to prevent the risk of DIC, but also to not increase the risk of coronary artery bypass graft failure or stents thrombosis. In association with unfractionated or low molecular weight heparin [6], we should use drugs that on the one hand do not promote DIC and on the other do not increase the risk of adverse cardiovascular events, i.e. cangrelor, bivalirudin. At this moment platelet and fresh frozen plasma transfusion, corticosteroids administration seem to be an effective therapy. Anti-Thrombin concentrate, prothrombin complex are also administered as prophylaxis of bleeding prevention. The concentration of factors present in the prothrombin complexes is approximately 25 times higher than that obtained in the fresh frozen plasma. Notably, besides its velocity of the response, the small volume of infusion provide a lower risk of respiratory complications associated with volume overload. Most statins undergo hepatic metabolism activation through CYP3A4, and concomitant administration of CYP3A4 inhibitors currently used in patients affected by COVID-19, such as ritonavir and cobicistat, could increase the risk of muscle and liver toxicity. Therefore, starting with a lower dose of statin and monitoring creatine-kinase and transaminases serum levels would be advisable in these cases. Most RCTs performed on patient taking statin treatment in presence of sepsis or ventilator-associated pneumonia failed to demonstrate a beneficial effect. Mehra et al. [7] have showed a better survival in COVID 19 patients treated with statins, but we cannot exclude the possibility of confounding factors, because of their study was not a randomized controlled trial. COVID 19 disease can occur more severely by affecting the lung parenchyma, but also because it can affect both the autoimmune and hematopoietic system. For these reasons, we should better define with future studies the diagnosis of the underlying pathology to be treated more effectively.

References

[1] Giuseppe Lippi, Mario Plebani, Brandon Michael Henry, Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis, Clin. Chim. Acta 506 (2020) 145–148, https://doi.org/10.1016/j.cca.2020.03.022.
[2] A. Ashoub, S. Lakshmanan, H. Luckraz, Cardiac surgery in a patient with severe thrombocytopenia: How low is too low? Ann. Card. Anaesth. 16 (2013) 147–150.
[3] K. Koltai, G. Kesmarky, G. Feher, A. Tibold, K. Toth, Platelet aggregometry testing: molecular mechanisms, techniques and clinical implications, Int. J. Mol. Sci. 18 (8) (2017) 1803, https://doi.org/10.3390/ijms18081803.
[4] M. Yang, M.H.L. Ng, C.K. Li, Thrombocytopenia in patients with severe acute respiratory syndrome (review), Hematology 10 (2005) 101–105, https://doi.org/10.1080/10245330400026170.
[5] H. Wada, T. Matsumoto, Y. Yamashita, Diagnosis and treatment of disseminated intravascular coagulation (DIC) according to four DIC guidelines, J. Intensive Care 2 (2014) 15, https://doi.org/10.1186/2052-0492-2-15.
[6] M.M. Samama, A.T. Cohen, J.Y. Darmon, et al., A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients; prophylaxis in medical patients with enoxaparin study group, N. Engl. J. Med. 341 (1999) 793–800, https://doi.org/10.1056/NEJM199909093411103.
[7] M.R. Mehra, S.S. Desai, S. Kuy, T.D. Henry, A.N. Patel, Cardiovascular disease, drug therapy, and mortality in Covid-19, N. Engl. J. Med. doi: 10.1056/NEJMoa2007621.

Dario Buioni*, Paolo Nardi, Giovanni Ruvolo
Cardiac Surgery Unit, University Policlinico Tor Vergata, Rome, Italy
E-mail address: docyuk@libero.it (D. Buioni).

* Corresponding author at: Cardiac Surgery Unit, University Policlinico Tor Vergata, viale Oxford 81, Rome 00133, Italy.

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