


Heparin-Related Major Bleeding in Covid-19-Positive Patient: Perspective from the Outbreak

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To the Editor

The Covid-19 pandemic, due to its rapid spread [1], is significant straining the various national health systems, especially due to the number of patients requiring long-term support in intensive care unit (ICU). Thus, governments have started massive healthcare unit expansion, supplying medical equipment and personal protective equipment as well as creating and/or converting existing

buildings into Covid dedicated field hospitals. These facilities have limited infrastructure, specifically no ability to perform complex imaged guided interventions.

The principal cause of death is acute respiratory insufficiency although concern exists over the concomitant coagulation disorder that can precipitate disseminated intravascular coagulation (DIC) [2]. In light of this, heparin therapy has been introduced recently as an adjuvant

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therapy, showing promising results (28 mortality day, heparin users vs nonusers [40.0% vs 64.2%, $P = 0.029$], respectively) [3]. A heparin regimen has been also suggested by International Society of Thrombosis and Haemostasis (ISTH) guidance [4]. Moreover, Covid-19-induced thrombocytopenia has been postulated as a direct or a sepsis-induced effect, increasing risk of bleeding. Between 23 March and 26 April, we referred 38 Covid-19-positive patients (median age 67.4 ± 12.9 ; 21 males [68.0%]) in 11 different Covid-19 hospitals in Italy, with a major bleeding receiving heparin at therapeutic dosages. Bleeding (single: 26/38 [68.4%]; multifocal 12/28 [42.8%]) was observed (admitted to the ICU (27/38 [71%]) that required emergency lifesaving embolization in an interventional radiology suite. The decision to proceed with the embolization rather than suspending heparin administration was weighted according to the patient's clinical condition. In 25/38 (65.7%) critically unwell patients who were judged to be higher the risk of Covid-19-induced DIC, it was believed unsafe to stop the heparin and endovascular embolization was performed. In 13/38 (34.2%) less compromised patients, it was deemed safe to stop heparin and embolization was performed in 6/13 (46.2%). In the remaining patients, a watch-and-wait strategy was observed. The majority of bleeding was intramuscular (34/38 [89.4%]), 1/38 (2.6%) cerebral arteriovenous malformation, 1/32 (2.6%) in the retroperitoneal space and 1/32 (2.6%) splenic. The occurrence of bleeding in this situation has several implications:

- Usually heparin-related bleeding resolves spontaneously at the suspension of the anticoagulation regimen. However, heparin is considered an integral part of Covid-19 treatment and essential in critically ill patients at the risk of DIC.
- A 24/7 fully operational angiographic suite (including angiographic equipment, physician, nurse and technician) should be mandatory in all highly affected Covid Hospitals.
- Bleeding patients usually require blood transfusion which is in short supply during the Covid pandemic due to the lockdown and fear of entering medical facilities
- Biocontainment transfer of Covid-19-positive patients within the hospital is complex and not easy to achieve [5]

In view of these considerations, interventional radiology plays a crucial role and a dedicated treatment pathway

should be set up. In this context, a dedicated Covid-19 Hub-Spoke system should be set up with a well-defined protocol for transport and case acceptance in order to avoid hospital spread and resource waste. In conclusion, although major bleeding seems to be rare in Covid-19 patients, its management is complex for several reasons: the need to continue anticoagulation, shortage of blood products, multiple sites of haemorrhage and logistic issues.

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Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Institutional Review Board (IRB) Approved the letter.

Informed Consent Informed consent was obtained from all individual participants included in the study.

Consent for Publication Consent for publication was obtained for every individual person's data included in the study

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