

# Transcatheter Arterial Embolization as a Treatment for Life-Threatening Retroperitoneal Hemorrhage in COVID-19 Patients on Anticoagulant Therapy

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## Abstract

Retroperitoneal hemorrhage is a possible complication that has been noticed in COVID-19 patients on anticoagulant therapy. The data related to treatment and outcomes in this condition are scarce. We present a case series of four COVID-19 patients with lumbar artery bleeding, who were treated with transcatheter arterial embolization using embolization particles. The procedure was executed without any complications, and hemostasis was achieved in all four patients. Despite the patients survived the procedure, one patient died due to respiratory failure three weeks after the procedure, and one died due to hypovolemic shock two days later. Considering the ongoing state of COVID-19 pandemic, it is essential to be aware of transcatheter arterial embolization as a safe and effective procedure for treating retroperitoneal hemorrhage in COVID-19 patients.

## Keywords

COVID-19, Retroperitoneal Hemorrhage, Lumbar Artery Bleeding, Transcatheter Arterial Embolization, Anticoagulant Therapy

## 1. Introduction

COVID-19 is an acute, complex disease that is caused by SARS-CoV-2 infection which in its most severe forms results in the development of interstitial pneumonia and acute respiratory distress syndrome (ARDS) [1] [2]. Apart from

ARDS, the high risk of thrombosis or bleeding in critically ill patients with COVID-19 has been noticed [3]. It was previously reported that direct SARS-CoV-2 infection of endothelial cells may be associated with hypercoagulability as well as diffuse blood clots (disseminated intravascular coagulation (DIC)) which are characterized by an increased risk of bleeding due to platelet and fibrinogen consumption [4]. DIC and large-vessel thrombosis have been linked to multi-system organ failure [5] [6]. To combat this hypercoagulable state, patients infected with COVID-19 should be properly anticoagulated to reduce ischemic risk. However, there are some evidence that anticoagulation treatment may cause life-threatening bleeding complications such as retroperitoneal hemorrhage [7] [8] [9].

It was published by Abate *et al.* that the incidence of spontaneous muscle hematoma is 3 - 4 times higher in patients with COVID-19 compared to patients on anticoagulant therapy who were not infected with COVID-19 [10]. The same authors reported a mortality of 32.4%, indicating that the occurrence of spontaneous muscle hematoma significantly worsens the prognosis of patients with COVID-19 [10]. We present four cases of retroperitoneal hemorrhage due to lumbar artery bleeding in patients being treated with anticoagulant therapy, emphasizing the importance of rational use of anticoagulation in COVID-19 patients as well as the need of rapid radiological investigation and treatment of bleeding by transcatheter arterial embolization (TAE).

## 2. Case Presentation

We experienced four patients (1, 2, 3, and 4) with retroperitoneal bleeding due to usage of nadroparin calcium (fraxiparine) as anticoagulant treatment in COVID-19 pneumonia. At the moment of admission, all of the patients presented with fever and respiratory symptoms and they were diagnosed with COVID-19 by RT-PCR.

Patients' characteristics are presented in **Table 1**.

**Table 1.** Patients' characteristics.

CASE	1	2	3	4
Age	69	65	83	71
Sex	Male	Male	Female	Female
Preexisting conditions <sup>a</sup>	None	CAD	CAD, DM type II, HT	None
CT severity <sup>b</sup> score	23	11	18	/

a. CAD-coronary artery disease, HT-hypertension, DM-diabetes mellitus. b. The CT severity score is a scoring system used to assess the lung changes and involvement by COVID-19. It is based on visualization of changes characteristic of COVID-19 (ground glass opacities, vascular enlargement, consolidation, subpleural band, architectural distortion, crazy paving) using native CT examination. The total CT score is the sum of the individual lobar scores and can range from 0 (no involvement) to 25 (maximum involvement), when all the five lobes show more than 75% involvement.

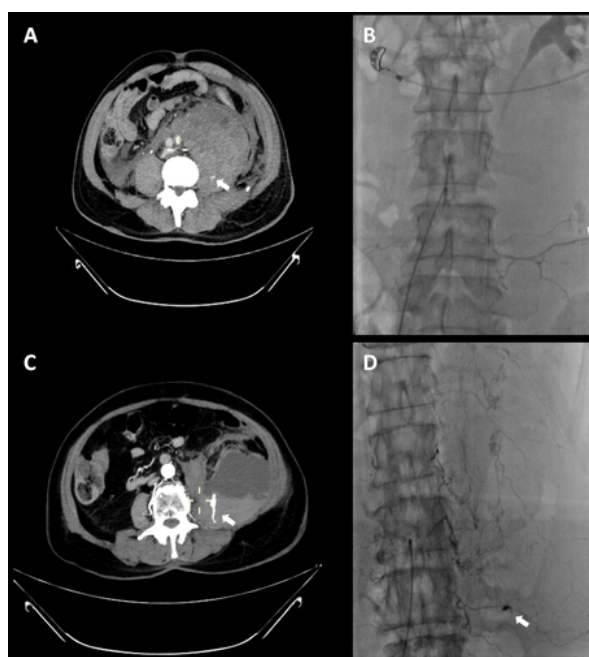
The patients included 2 men and 2 women (average age, 72 years). Patients were hospitalized due to COVID-19 pneumonia that was confirmed by CT scanning without intravenous contrast for three of them (1, 2, 3). Their CT severity scores were 23, 11, and 18, for 1, 2, and 3, respectively. Two patients (2, 3) with previously diagnosed coronary artery disease were continued on aspirin and all four of them were started on prophylactic fraxiparine (5700 i.j./0.6 mL/daily s.c.) due to concern about COVID-19 induced hypercoagulable state. Over the course of hospitalization, all of the patients showed a drop in hemoglobin levels, and conservative treatment was applied accordingly. Despite the blood transfusions, after 2 to 3 days all of the patients had continuous hemoglobin levels drop ( $>35$  g/L), and became hemodynamically unstable.

The average values of hemoglobin, platelet count, prothrombin time (international normalized ratio), and the activated partial thromboplastin (aPTT) time, before interventions, were 64.5 g/L,  $149 \times 10^9/L$ , 1.2, and 23.4 seconds, respectively (**Table 2**).

Retroperitoneal bleeding was diagnosed in all patients by computed tomography (CT) imaging, and no vessel malformations such as aneurysm, arteriovenous malformation, or arteriovenous shunt were found. CT images showed that all patients (1 - 4) had retroperitoneal collection of blood involving the ilio-psoas muscle. Active extravasation of contrast medium was detected in CT scans (**Figure 1(A)** and **Figure 1(C)**). Continuous drop in hemoglobin levels, hemodynamic instability, active extravasation of contrast on CT scans and current use of anticoagulation, were indications for TAE. In all four patients, the common femoral artery was accessed using Seldinger method and selective angiography of lumbar arteries was performed. Extravasation of contrast medium was identified from branches of the lumbar arteries (**Table 3**), visualized as “blush” outside the vessel (**Figure 1(B)** and **Figure 1(D)**). Hemostasis in all four patients was achieved with superselective microcatheter embolization using embolization particles (Hydropearl™). Hydropearl™ microspheres are polyethylene glycol (PEG) microspheres, for accurate embolization at the target area (**Table 3**). Care was taken to slowly infuse the particles with low-pressure hand injections while monitoring for reflux on fluoroscopy. The retrograde flow was not observed during the embolization procedure. Postembolization arteriography confirmed occlusion of the embolized vessel.

**Table 2.** Laboratory findings.

CASE	1	2	3	4
HGB (g/L)	59	81	62	56
Platelet count ( $10^9/L$ )	88	75	356	77
Prothrombin time (INR)	1.29	1.02	0.92	1.57
aPTT (seconds)	27.1	20.7	18.3	27.5



**Figure 1.** Representative images of computed tomography scan of the abdomen and pelvis demonstrating a giant intramuscular hematoma in the iliopsoas muscle and the active bleeding point (white arrowheads) ((A) and (C)). Angiographic image demonstrating extravasation of contrast medium seen as “blush” outside the vessel (white arrowheads) ((B) and (D)).

**Table 3.** Radiological findings and intervention characteristics.

CASE	1	2	3	4
Hematoma size (mm)	210 × 70	143 × 164	45 × 190	100 × 90
Occluded arteries	Left lumbar artery (L3)	Left lumbar arteries (both)	Right lumbar arteries (L2, L3, L4)	Left lumbar artery (L3)
Hydropearl Total volume (ml)	4	4	8	4
Size (µm)	400	600	400	400
OUTCOME	Death	Survival	Survival	Death

Two (2 and 3) of the four patients are still alive at one and two months, respectively, after the intervention. Unfortunately, patient 1 died due to hemodynamic instability two days after the intervention. Patient 4 remained in ICU due to COVID-19 pneumonia with a stable hemoglobin level and no further bleeding, but eventually died due to respiratory failure three weeks after the intervention.

### 3. Discussion

High mortality in patients suffering from COVID-19 as multi-systematic disease

is caused by multiple factors, including hypercoagulable phenomenon. Elevated pro-inflammatory cytokine levels, mainly IL-6 are associated with this hypercoagulable state by promoting atherosclerotic changes through hemodynamic changes, local inflammation, and plaque rupture [11] [12]. Thus, patients with COVID-19 may present with acute thrombotic complications affecting different organ systems. Although, prophylactic anticoagulant therapy is recommended and proved to be beneficial, some bleeding complications have been reported [12] [13]. First case of enoxaparin-induced spontaneous lumbar artery bleeding was reported by Sun and colleagues in 2009. It was successfully treated with TAE and hemodynamic stability was regained [14]. Recently, Patel and coworkers [12] published a case report about COVID-19 patient with life-threatening psoas hematoma on enoxaparin, who was successfully treated with arterial embolization, suggesting that TAE is safe, minimally invasive procedure with prompt therapeutic effect. Moreover, the interventional management of spontaneous soft tissue hematoma in COVID-19 patients was reported by Lucatelli *et al.*, confirming TAE as a superior therapeutic approach in comparison to conservative treatment [8] [9]. The results presented in our case series are in agreement with previously published findings that TAE is promising therapeutic option in anticoagulated patients [12] [15] [16].

All 4 patients in our study survived TAE procedure, but one (1) died of ARDS induced by COVID-19 pneumonia, three weeks later. The death of another patient (1) was caused by bleeding-related cardiovascular failure, furthermore suggesting the significance of prompt radiologic investigation and intervention. These findings are in agreement with recommendations regarding prompt angiographic management of retroperitoneal hemorrhage in COVID-19 patients, previously reported by Lucatelli *et al.* [8] [9]. Since the data related to retroperitoneal bleeding in COVID-19 patients and its management is very scarce, the presented and similar reports provide a significant contribution in this field.

#### 4. Conclusion

Considering that COVID-19 pandemic has led to a dramatic loss of human life worldwide and presents an unprecedented challenge to public health, it is of great significance for clinicians to be aware of possible complications, such as retroperitoneal hemorrhage, and to be able to recognize the symptoms. Early radiological detection and proper treatment, such as TAE, is the way to lower mortality due to retroperitoneal hemorrhage.

#### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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