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SHORT COMMUNICATION COVID-19

Spontaneous Haematomas in Anticoagulated Covid-19 Patients: Diagnosis and Treatment by Embolization

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Abstract
Purpose To assess the safety and efficacy of embolization for spontaneous bleeding in anticoagulated patients with COVID-19.
Material and Methods Single center retrospective study in 9 patients with COVID-19 who experienced bleeding complications following anticoagulation. The study included 8 men and 1 woman aged from 48 to 80 years (mean 69.7 years), who had a total of 10 soft tissue haematomas: 1 in the thigh, 1 in the anterior abdominal wall, 6 retroperitoneal and 2 thoracic haematomas. All patients were referenced for vascular embolization, mostly with Onyx-18.
Results A total of 10 haematomas were embolized in 9 patients. Technical success was achieved in all patients. No complications or adverse events were noted. One patient required percutaneous drainage of an infected haematoma 88 days after embolization. The mean hemoglobin level before embolization was 8,64 mg/dL and increased to 9,08 mg/dL after embolization (p = 0,3). After embolization all patients recovered haemodynamic stability and blood pressure levels improved. Seven patients resumed anticoagulation therapy after embolization. There were no recurrences or new bleedings in all treated patients. No patients required any additional invasive therapies or surgery. Mean intensive unit care and hospital stay was 6.7 and 35.2 days, respectively. All patients were discharged and were well at follow-up clinic visits 2–7 months after embolization. Seven patients performed a control CT scan 1–6 months after embolization, showing complete resolution of the haematoma.
Conclusion Embolization is safe and effective to treat spontaneous haematomas in anticoagulated patients with COVID-19, allowing to resume anticoagulation therapy.
Level of evidence IV Level 4, case-series.

Keywords Spontaneous haematoma · Active bleeding · COVID-19 · CT angiography · Embolization · Onyx · EVOH

Introduction

Bleeding complications in elderly patients on anticoagulant therapy are estimated at about 5%, [1] with an incidence of spontaneous haematomas of about 0.6%. [1] In large haematomas with hemodynamic instability, the prognosis is poor with multiple organ failure, [2] reaching a mortality of 30–50%. [3, 4] COVID-19 infection causes a disorder of haemostasis, [5] with a procoagulant state. This has led to the inclusion of thromboprophylactic (anticoagulant) therapy in most treatment protocols. [2–10] Recent studies refer to heparin-induced thrombocytopenia, [6, 10] and a percentage of patients develop renal failure in the coronavirus infection. This results in an increased half-life of heparin, which circulates in the plasma longer, [8] leading to "pseudo-overdosing", increasing the risk of bleeding. In COVID-19 patients, the incidence of haematomas appears to be higher due to coagulation disorders caused by

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infection, coupled with thrombocytopenia due to heparin and overdose in patients with renal failure.

Computed tomography (CT) angiography is essential to the diagnosis of haematomas as it allows the size, location and artery responsible for the bleeding to be establised, [11] identifying the location of the vascular origin of the bleeding in 95,2% of cases. [1]

The purpose of the study was assess the safety and efficacy of embolization for spontaneous bleeding in anticoagulated patients with COVID-19.

Material and Methods

Single center retrospective study in 9 patients with COVID-19 who experienced bleeding complications following anticoagulation.

The study included 9 patients, 8 men and 1 woman, aged from 48 to 80 years (mean 69.7 years), who had a total of 10 soft tissue haematomas: 1 in the thigh, 1 in the anterior abdominal wall, 6 retroperitoneal and 2 thoracic haematomas, with signs of active bleeding on CT angiography (Figs. 1 and 2). All patients included were receiving anticoagulant therapy. Other clinical variables were also collected and included in Table 1.

All patients were referenced for vascular embolization.

Imaging Protocol

Patients with clinically suspected active bleeding underwent CT angiography of the chest or abdomen, following a three-phase or two-phase protocol of the radiologist´s choice. All studies were performed on a General Electrics Revolution EVO (General Electrics Healthcare, Chicago, Illinois) or Philips Brillance (Philips Healthcare, Cleveland, Ohio) 64-row multidetector computed tomography (MDCT).

Iodinated contrast medium Omnipaque 300 (General Electrics Healthcare, Chicago, Illinois) was used, with 60 ml for thoracic studies and 80–100 ml for abdominal studies. In patients with kidney failure, Visipaque 320 (General Electrics Healthcare, Chicago, Illinois) was used.

CT angiography confirmed haematoma with active bleeding in 9 patients, one of them with 2 concomitant haematomas. The location, size of the haematoma and the artery responsible for the bleeding are detailed in Table 2.

Endovascular Treatment

The embolization procedure was performed with a General Electrics Innova 4100 angiographic system (General Electrics Healthcare, Chicago, Illinois). A right or left femoral vascular access was preferentially performed. In

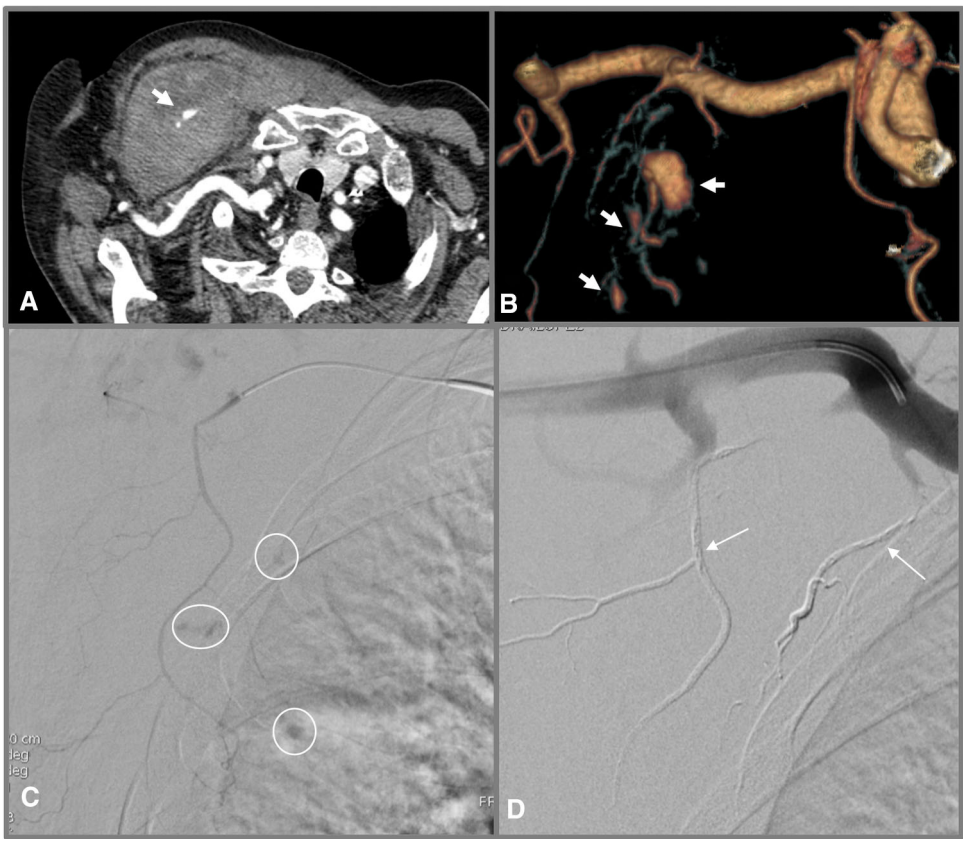

Fig. 1 (case 5) **a** (MDCT) and **b** (VR reconstruction) Right pectoral haematoma with active bleeding (short arrow). **c** Arteriography of the lateral thoracic branch with contrast extravasation (circle). **d** Control after embolization of lateral thoracic and thoracoacromial branches, with no contrast extravasation, with Onyx-18 cast (long arrow)

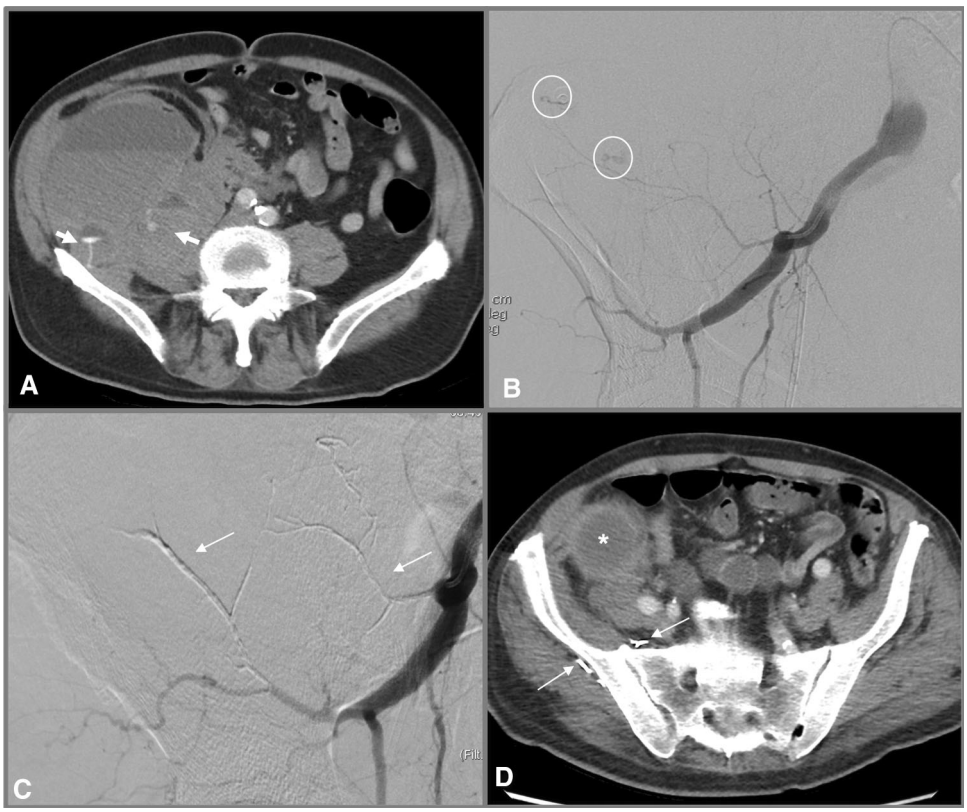

Fig. 2 (case 6) **a** MDCT, haematoma in the right iliopsoas with active bleeding (short arrow). **b** Iliolumbar artery arteriography with contrast extravasation (circle). **c** Control after embolization of the iliolumbar artery and superior gluteal terminal branch, with no contrast extravasation, with Onyx-18 cast (long arrow). D Follow-up CT 88 days after embolization, decreased haematoma size, ring-shaped enhancement indicative of infection (asterisk) and Onyx-18 in embolised arteries (long arrow)

all cases a 5F introducer sheath (Terumo, Shibuya-Ku, Tokyo) was used. The catheters used were: Multi-purpose 4F (Cordis, Miami, FL), Cobra 2 4F (Cordis, Miami, FL) or Simmons 1 4F (Cordis, Miami, FL). The microcatheters used were Progreat 2.7 (Terumo, Shibuya-Ku, Tokyo) or Rebar 18 (Covidien Medtronic, Irvine, CA).

The choice of embolising agent was based at the operator´s preferences. The embolization material was Ethylene–Vinyl Alcohol (EVOH) Copolymer Onyx-18 (Covidien Medtronic, Irvine, CA) in 7 cases (Fig. 1 and Fig. 2), one of them in combination with Gelita-Spon Powder (Absorbable Gelatin Powder Hemostat) (Gelita Medical, Eberbach, Germany). Pushable microcoils (Interlock 2D (Boston Scientific, Malborough, MA) and Hilal embolization microcoils (COOK Medical´s, Bloomington, IN)) were used in one case. Glubran2 (N-butyl-2-cyanocrylate (NBCA)) (GEM, Viareggio, Italy) was used in one case. Gelita-Spon Powder (Gelita Medical, Eberbach, Germany) was used in one case. The treatments and materials used are detailed in Table 2.

Results

In the study, CT angiography detected active bleeding in all cases, assessed haematoma volume and severity of clinical status.

The study, in line with current literature, shows a predominance of spontaneous haematomas, with a total of 10 soft tissue haematomas, which were embolised in 9 patients. In the context of coagulation disorders, it was decided in most cases to treat with a liquid embolic agents, predominantly Onyx-18.

Technical success was achieved in all cases, without complications during or after the embolization procedure.

The mean hemoglobin level before embolization was 8,64 mg/dL and increased to 9,08 mg/dL after embolization with standard deviation of 1.3 ($p = 0.3$).

There were no recurrences or new bleedings in all treated patients. None of them required surgery. Seven patients resumed anticoagulation therapy after embolization (Table 1).

Mean intensive unit care (ICU) and hospital stay was 6.7 and 35.2 days, respectively. All patients experienced a progressive improvement until they were discharged.

Seven patients performed a control CT one month and 6 months after embolization, showing resolution of all treated haematomas. One patient required percutaneous drainage of an infected haematoma 88 days after embolization (Fig. 2).

Eight patients were reviewed in consultation at 2 and 7 months and were asymptomatic.

Table 1 Demographic and laboratory

Case	Sex	Age	Cr	DD	Fibrinogen	Inflamatory markers	Platelets	Coagulation	Hb	Hb reduction	Hb after embolization	Anticoagulant therapy	Resumption of anticoagulant therapy	Days to resume	Days of ICU/ hospital admission	Discharge date	Control CT
1	M	48	1,4	4607	316	F 1754	186,000	PA 64%	7,9	3,9	9,5	Enoxaparin	No	–	7/36	17/4/2020	–
						PCR 395		INR 1,36				80 mg/12 h					
2	M	69	2,7	682	318	F 1723	154,000	PA 69%	5,7	6,8	8	Enoxaparin	Enoxaparin	25	15/30	25/4/2020	19/10/ 2020
						PCR 30		INR 1,28				60 mg/12 h	60 mg/24 h				
3	M	60	1,79	6349	316	F 1505	164,000	PA 78%	6,9	6,4	7,2	Enoxaparin	Enoxaparin	11	20/29	11/5/2020	23/11/ 2020
						PCR 2,2		INR 1,17				80 mg/12 h	40 mg/24 h				
4	M	66	0,5	929	351	F 723	80,000	PA 55%	9	2	9,3	Enoxaparin	Enoxaparin	2	3/46	12/5/2020	5/11/ 2020
						PCR 3,7		INR 1,5				60 mg/12 h	80 mg/24 h				
5	M	80	1,2	2280	877	F 410	286,000	PA 65%	9	1,6	9,9	Enoxaparin	Enoxaparin	8	2/27	5/8/2020	7/9/ 2020
						PCR 100		INR 1,3				80 mg/12 h	80 mg/24 h				
6	M	71	1,9	1350	183	F 11,666	175,000	PA 58%	9,8	1,9	9,5	Enoxaparin	No	–	2/37	15/10/ 2020	23/4/ 2021
						PCR 3,3		INR 1,4				80 mg/12 h					
7	F	79	1,06	742	421	F 1340	237,000	PA 44%	9,5	2,5	9	Enoxaparin	Enoxaparin	8	2/39	20/2/2021	13/8/ 2021
						PCR 128		INR 1,9				80 mg/12 h	60 mg/24 h				
8	M	77	1,4	901	196	F 496	117,000	PA 74%	11,7	1,3	9,6	Enoxaparin	Enoxaparin	9	4/40	22/2/2021	9/8/ 2021
						PCR 3,8		INR 1,2				60 mg/12 h	40 mg/12 h				
9	M	78	0,48	2024	308	F 3839	243,000	PA 72%	8,3	1,2	9,7	Enoxaparin	Enoxaparin	15	5/33	27/2/2021	7/6/ 2021
						PCR 91		INR 1,2				80 mg/12 h	40 mg/24 h				

Sex (M: male, F: female), age: years, Cr (creatinine): mg/dL, DD (D-dimer): mcg/l, fibrinogen: mg/dL, F (ferritin): ng/dL, CRP (C reactive protein): mg/L, platelets: 10^3/mcl, PA (prothrombin activity): %, INR (international normalised ratio), Hb (haemoglobin): g/dL (at the time of bleeding), Hb reduction (haemoglobin reduction): points of haemoglobin reduction from the previous laboratory tests, Hb after embolization (24 h): g/dL, Anticoagulant therapy (at the time of bleeding), Resumption of anticoagulant therapy: treatment and doses, Days to resume: days to resume the anticoagulant therapy after embolization, Days of ICU (Intensive Care Unit)/hospital admission, Discharge date: clinical discharge date, Control CT: date of follow-up CT scan showing resolution of haematoma

Table 2 Description of the haematomas and treatment

Case	Haematoma location	Haematoma size *	Artery responsible for bleeding	Embolization materials
1	Right psoas muscle	10 × 12 × 10	4th lumbar	Onyx-18
2	Right psoas muscle	14 × 8 × 18	3rd lumbar and 4th lumbar	Microcoils
3	Right iliacus psoas muscle	11 × 9 × 13	Iliolumbar	Glubran2
4	Right thoracic wall	8 × 7 × 17	Subscapularis and lateral thoracic	Onyx-18
	Left psoas muscle	7 × 9 × 10	Iliolumbar	Onyx-18
5	Right pectoral muscle	8 × 9 × 13	Thoracic branches of subclavian	Onyx-18
6	Right iliacus psoas muscle	12 × 12 × 19	Iliolumbar and superior gluteal	Onyx-18
7	Left anterior rectus muscle	14 × 11 × 9	Inferior epigastric	Gelita-spon Powder
8	Right iliacus psoas muscle	4 × 3 × 8	3rd lumbar and 4th lumbar	Onyx-18
9	Left thigh	10 × 12 × 17	Deep femoral	Onyx-10 and Gelita-spon Powder

*Measures: centimeters (cm) transverse x cm anteroposterior x cm craniocaudal

Discussion

Endovascular treatment with embolization of the arterial contributions of the haematoma is a minimally invasive, safe and effective technique, less invasive and more selective than surgery, [2, 3] with a technical success of 90%. [1] It is currently the technique of choice for the treatment of active arterial bleeding, as it does not carry the disadvantages associated with surgery. Patients have an early recovery, with a shortened hospital and ICU stay. [10] Recurrence after embolization is rare and usually occurs in patients with severe consumptive coagulopathy. [1]

There are different materials and devices to perform embolization, and the selection of one over another depends on multiple factors, such as characteristics of bleeding (morphology and caliber of the responsible artery), the ability to access the bleeding site ("local" or "distant" embolization), the operator´s experience with the different materials and others inherent to patient's condition (existence of coagulopathy, etc.). There are now retrospective studies suggesting the advantages of liquid embolic agents as they provide rapid complete occlusion compared to others such as coils. [12]

In the study, most of the embolization were performed with Onyx-18 (Table 2). The selection of this material was mainly based on two factors, on the one hand the morphology of the responsible artery, in all cases small calibre arteries, and on the other hand the presence of a coagulation disorder. Onyx-18 is a non-adhesive permanent liquid emboliser that allows complete, rapid and safe vascular occlusion of the vascular lumen by polymerization, especially in patients with coagulation disorders (unlike other materials that require coagulation activation to achieve effective vascular closure). It allows complete control, with no microcatheter adherence or migration of embolization material. No special preparation is required for COVID-19 patients.

Conclusion

Bleeding complications in COVID-19 patients are a major cause of increased morbidity and mortality in these patients. Utmost care should be taken in COVID-19 patients treated with heparin at therapeutic doses, avoiding the risk of overdosing.

In cases of suspected active bleeding, early diagnosis and treatment are essential to ensure patient survival. CT angiography is the diagnostic tool of choice.

Embolization is safe and effective to treat spontaneous haematomas in anticoagulated patients with COVID-19,

allowing to resume anticoagulation therapy and should be considered as first choice treatment. Onyx-18 is a rapid and safe vascular occluder, particularly in patients with coagulation disorders.

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Declarations

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

Consent for Publication For this type of study consent for publication is not required.

Ethical Approval For this type of study formal consent is not required.

Informed Consent For this type of study informed consent is not required.

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