Vaccination strategies have been at the forefront of controlling the COVID-19 pandemic. An association between vaccine-induced immune thrombotic thrombocytopenia (VITT) and one of these vaccines, the ChAdOx1 nCov-19 vaccine, is now recognized (2–5). The purpose of this study was to investigate the frequency and location of thrombosis in each vascular system using CT, MRI, and US to identify additional sites of thrombus in a United Kingdom–wide sample of patients with confirmed VITT. Thirty-two radiology centers identified through the national collaborative Radiology Academic Network for Trainees were invited from the United Kingdom; seven of these contributed to this study. All patients with confirmed VITT between February 3 and May 12, 2021, who met the inclusion criteria were included. The location and extent of thrombi were evaluated using CT, MRI, and US. A total of 40 patients (median age, 41 years [IQR, 32–52]; 22 [55%] men) with confirmed vaccine-induced immune thrombotic thrombocytopenia after administration of their first ChAdOx1 nCov-19 vaccine were included. Thirty-two patients (80%) developed symptoms within the first 14 days, and eight (20%) developed symptoms within 14–28 days. Twenty-nine patients (72%) experienced neurological symptoms and were confirmed to have cerebral venous sinus thrombosis, 12 (30%) had clinical deterioration and repeat imaging demonstrated extension of their primary thrombus, and eight (20%) died. Twenty-five of 30 patients (83%) who underwent additional imaging had occult thrombosis. In conclusion, patients with VITT are likely to have multiple sites of thrombosis, with the most frequent being cerebral venous sinus thrombosis in combination with pulmonary embolism and portomesenteric venous thrombosis. Whole-body imaging with contrast-enhanced CT can be used to identify occult thrombosis.

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seven of these contributed to this study. All patients with confirmed VITT between February 3 and May 12, 2021, who met the inclusion criteria were included.

The inclusion criteria were presentation within 28 days after administration of the ChAdOx1 nCov-19 vaccine, presence of anti-PF4 antibodies, thrombocytopenia (platelet count <150 × 10^9/L), and new radiologically confirmed thrombosis on at least one contrast-enhanced CT scan. Exclusion criteria were a history of thrombophilia, a polymerase chain reaction serologic test positive for COVID-19, and unavailable PF4 antibody testing or imaging information.

Patients were identified through a search of local hematology databases, anti-PF4 testing, and cross-referencing with imaging findings on a local picture archiving and communication systems workstation. The electronic health record for each included case was reviewed to collect demographic data, clinical information, laboratory results, and outcomes (Table E1 [online]). Patient characteristics and clinical, biochemical, and imaging information were recorded on standardized data collection sheets. Imaging was reviewed locally by unblinded consultant radiologists or senior radiology trainees (J.Y., A.G., I.W., A.K., A.M., S.G., C.v.S.; ≥4 years of experience in cross-sectional imaging).

CT, MRI, and US were performed according to local hospital protocols (Table 1). The aforementioned readers commented on thrombus to a subsegmental level, where possible, in the following vascular systems (Table 2): (a) cerebral venous sinus thrombosis (CVST), (b) systemic deep venous thrombosis (lower limb deep venous thrombosis; inferior and superior vena cava; and hepatic, renal, and adrenal veins), (c) portomesenteric venous thrombosis (PVT) (portal, superior, and inferior mesenteric and splenic veins), (d) systemic arterial thrombosis (including intracranial and visceral arterial thrombosis), and (e) pulmonary embolism (PE).

Images were stratified into three categories: cerebral imaging (head CT, brain MRI, and venogram CT), whole-body imaging (chest, abdominal, and pelvic CT), and partial-body imaging (any patient who did not undergo complete chest, abdominal, and pelvic CT, which included focused US assessment).

### Statistical Analysis

Descriptive statistics were used to describe proportions of scans or patients with thrombus at each anatomic site us-

| Table 1: Imaging Modality within 48 Hours of Admission in Relation to Presenting Symptoms |
|---------------------------------------------------------------|
| Symptom           | CT Head and CT or MRI Venogram | CT Pulmonary Angiogram | CT Abdomen and Pelvis with Contrast Material | CT Chest, Abdomen, and Pelvis with Contrast Material or CT Aortogram | MRI Abdomen with Contrast Material | US Duplex Abdomen | US Duplex Peripheral Veins |
|--------------------|---------------------------------|------------------------|---------------------------------------------|-----------------------------------------------------------------|---------------------------------|------------------|--------------------------|
| Neurologic (n = 29) | 29 (100)                        | 9 (11)                 | 6 (21)                                      | 9 (11)                                                          | 0                               | 2 (7)            | 2 (7)                    |
| Gastrointestinal (n = 4) | 4 (100)                        | 2 (50)                 | 2 (50)                                      | 2 (50)                                                          | 1 (25)                          | 0                | 0                        |
| Chest (n = 6)      | 5 (83)                          | 4 (67)                 | 1 (17)                                      | 3 (50)                                                          | 0                               | 1 (17)           | 0                        |
| Other* (n = 1)     | 1 (100)                         | 0                      | 0                                           | 1 (100)                                                        | 0                               | 0                | 0                        |
| Total (n = 40)     | 39 (98)                         | 15 (37)                | 9 (22)                                      | 15 (37)                                                        | 1 (2)                           | 3 (8)            | 2 (5)                    |

Note.—Data are number of patients, and data in parentheses are percentages. * “Other” includes pyrexia and night sweats.

| Table 2: Site of Vascular Thrombus after ChAdOx1 nCov-19 Vaccination in Relation to Presenting Symptom |
|---------------------------------------------------------------------------------------------------------|
| Symptom                                                   | Pulmonary Embolism | Portosystemic Venous Thrombosis | Cerebral Venous Sinus Thrombosis | Deep Venous Thrombosis | Systemic Arterial Thrombosis |
|-----------------------------------------------------------|-------------------|-------------------------------|--------------------------------|------------------------|-------------------------------|
| Neurologic (n = 29)                                      | 12 (41)           | 5 (17)                        | 29 (100)                       | 6 (21)                 | 4 (14)                        |
| Gastrointestinal (n = 4)                                 | 1 (25)            | 2 (50)                        | 2 (50)                         | 3 (75)                 | 1 (25)                        |
| Chest (n = 6)                                            | 4 (67)            | 2 (33)                        | 3 (50)                         | 1 (17)                 | 3 (50)                        |
| Other* (n = 1)                                           | 1 (100)           | 1 (100)                       | 0                              | 0                      | 0                             |
| Total (n = 40)                                           | 18 (45)           | 10 (25)                       | 34 (85)                        | 10 (25)                | 8 (20)                        |

Note.—Data are number of patients, and data in parentheses are percentages. * “Other” includes pyrexia and night sweats.
Thrombus Distribution in Immune Thrombotic Thrombocytopenia after Vaccination

Results

Patient Characteristics
Between February 3 and May 12, 2021, 40 patients from seven different centers across the United Kingdom met the inclusion criteria (Table E1 [online]). The median age was 41 years (IQR, 32–52; range, 21–66 years); 22 patients (55%) were men and 18 (45%) were women. Thirty-two patients (80%) developed symptoms within 14 days of their first ChAdOx1 nCov-19 vaccine, and eight patients (20%) presented 14–28 days after vaccination. None of the patients had received their second vaccine dose at presentation (Table E1 [online]).

Sites and Multiplicity of Thrombus across All Patients
At presentation, 10 patients (25%) underwent targeted imaging based on symptoms alone; 30 patients (75%) underwent additional imaging as will be detailed (Table 1). Whole-body imaging with contrast-enhanced axial CT was performed in 26 patients (65%) and partial-body imaging was performed in four (10%) within 48 hours of admission.

Further imaging during the study period identified additional sites of thrombosis in 25 of 30 patients (83%) who underwent additional imaging. The most common additional sites were a combination of CVST and PE in 16 of 40 patients (40%) or CVST and PVT in nine of 40 patients (23%). The total numbers of thromboses identified in each

Figure 1: Multimodality images in a 28-year-old woman who presented with headache and subsequent collapse. Cerebral venous sinus thrombosis was diagnosed, and whole-body imaging demonstrated large-volume splanchnic vein thrombosis, which was treated with transjugular intrahepatic portosystemic shunt insertion and catheter-directed thrombolysis. (A) Susceptibility-weighted axial brain MRI scan shows a thrombosed internal cerebral vein branch leading to the straight sinus (arrow). (B) Unenhanced axial head CT scan shows hyperattenuating clot within the cortical vein and transverse sinuses (arrow). (C) Coronal portal venous phase abdominal CT scan shows thrombosed portal and superior mesenteric veins (arrow). (D) Fluoroscopic angiogram obtained by injecting contrast material via a thromboaspiration catheter (red arrow) within the partially occluded superior mesenteric vein through a transjugular intrahepatic portosystemic shunt (between white arrows). Contrast material can be seen filling some segmental superior mesenteric vein branches, with several filling defects in the confluence of the portal vein. (E) Photograph of the thrombus cast of the superior mesenteric vein and portal vein aspirated from the splanchnic system via the portosystemic shunt using an aspiration thrombectomy catheter (Indigo, Penumbra).
vascular system across all 40 patients were 34 CVSTs (85%), 17 PEs (42%), 10 PVTs (25%), 11 deep venous thromboses (28%), and eight systemic arterial thromboses (20%).

Analysis by Mode of Presentation

A total of 29 patients (72%) presented with predominantly neurologic symptoms (Figs 1–3), including severe headache, blurred vision, seizure, or collapse. In all 29 patients, CT or MR venography depicted CVST (Table 2). In 15 of 29 patients (52%), intracranial hemorrhage was an associated finding and was bilateral in three of 15 patients (20%). Further imaging was completed in 20 of 29 patients (69%), with whole-body imaging in 17 (85%) and partial-body imaging in three (15%). In these 20 patients, additional sites of thrombus were identified in 17 (85%): PE in 12 (60%), PVT in five (25%), deep venous thrombosis in six (30%), and systemic arterial thrombosis in four (20%).

Six of 40 patients (15%) presented with thoracic symptoms of dyspnea, cough, chest pain, or hemoptysis. In all six patients, PE or intracardiac or coronary thrombus was confirmed (Table 2). Further imaging was performed in five of six (83%) of these patients. Of these five, one (20%) had solitary PE, three (60%) had additional CVST, and three (60%) had additional intraabdominal thrombosis (PVT and deep venous thrombosis).

Four of 40 patients (10%) presented with gastrointestinal symptoms, including abdominal pain, vomiting, and rectal bleeding. In all four patients, an intraabdominal thrombosis was found (Table 2): two with PVT (50%) and two with adrenal and renal vein thrombosis (50%). Further imaging in these four patients revealed that two patients had CVST
(50%), one had PE (25%), and one had combined CVST and intracranial arterial thrombosis (25%).

In all patients with occult PVT and PE, clinical monitoring was undertaken, and serial imaging was indicated if there were clinical signs of developing venous bowel ischemia or right-sided heart strain.

**Treatment**

Treatments consisted of anticoagulation, plasma exchange, steroid therapy, and intravenous administration of immunoglobulins. Of 40 patients, seven (18%) underwent platelet transfusion and one (2%) received 25-mg eltrombopag tablets (Revolade; Novartis Pharmaceuticals). Two patients (5%) with splanchic venous occlusion and compromised small bowel were transferred to tertiary hepatobiliary centers for further care (Table E1 [online]).

**Patient Outcomes**

Median follow-up was 44 days; during this period, eight of 40 patients (20%) died, all of them from brain herniation secondary to large-volume cerebral edema. Twelve of 40 patients (30%) had clinical deterioration and underwent repeat imaging. In eight of these 12 patients (67%), this showed extension of intracranial thrombus; in the remaining four (33%), there was extension of thrombus in a second vascular system. Of the four patients with progressing thrombus, two (50%) died of complications of VITT.

**Discussion**

International guidance suggests symptom-specific imaging for vaccine-induced immune thrombotic thrombocytopenia (VITT), but a paucity of data remains on the prevalence of multisite thrombosis and the implications of this on management. To our knowledge, this is the largest study to date of patients with VITT with whole-body imaging and multisystem thrombosis.

In 25 of 40 patients undergoing additional imaging (imaging in addition to that focused on the presenting site), most patients (83%) had thrombosis at an additional

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**Figure 3:** Images in a 56-year-old man with sudden loss of consciousness 2 weeks after vaccination for COVID-19 and who was subsequently diagnosed with vaccine-induced immune thrombotic thrombocytopenia. (A) Axial contrast-enhanced maximum intensity projection CT venogram shows occlusive thrombus within the left transverse sinus (white arrow) and adjacent large-volume parenchymal hemorrhage in the left parietal lobe (red arrow). Subsequent whole-body imaging was performed. (B) Axial CT pulmonary angiogram shows a segmental pulmonary embolism (white arrow) and peripheral upper lobe infarct (red arrow). (C) Coronal contrast-enhanced abdominal CT scan shows a large-volume main and right portal vein thrombosis (white arrow) and hepatic vein thrombosis (red arrow). (D) Axial image from the same study as C shows hepatic vein thrombus in the middle and right hepatic veins (arrows).
site. This is much higher than the reported diagnoses of VITT, where multisite thrombosis was seen in 27%–50% of patients, likely reflecting the fact that in many of these studies, comprehensive whole-body imaging was not performed (2–4,16–20). In our study, progressive thrombosis was observed within the first 7 days after presentation in a substantial proportion of patients. The overall mortality in our study sample was 20%, and mortality in those with confirmed progressive thrombosis was 50%. These findings emphasize that VITT is a multisystem disorder and suggest that whole-body contrast-enhanced imaging is likely to lead to identification of further thrombosis.

Additional imaging was performed in 30 of 40 patients (75%), mostly with CT pulmonary angiography or CT of the abdomen and pelvis. For example, in patients who present with neurologic symptoms secondary to VITT and CVST, signs and symptoms of developing splanchnic venous thrombosis may be overlooked. Whole-body imaging can be used to identify patients who require early referral to specialist vascular or hepatobiliary centers for catheter-directed thrombolysis or transjugular intrahepatic portosystemic shunt placement, for instance (10,21).

A strength of our study was the involvement of the Radiology Academic Network for Trainees to identify many patients across the United Kingdom. The retrospective study design imposed some limitations: Patients were excluded if specific hematologic (PF4 antibody) testing or imaging information was unavailable, and inclusion was limited to symptomatic patients presenting to a hospital. To date, having patients undergo imaging for asymptomatic thrombosis in VITT is not within routine clinical practice in the United Kingdom. It is therefore possible that in instances of limited whole-body imaging, the number of occult thromboses may be considerably higher than reported.

In conclusion, patients with vaccine-induced immune thrombocytopenia are likely to present with multiple sites of thrombosis, most frequently cerebral venous sinus thrombosis in combination with pulmonary embolism and portomesenteric venous thrombosis. Whole-body imaging with contrast-enhanced CT imaging can enable identification of occult thrombosis.

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