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Iodine-stained fragmented thromboembolism

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Abstract

Aim: Iodine-stained fragmented thromboembolism (ISFT) is a rare phenomenon encountered in the immediate aftermath of mechanical thrombectomy or rarely as a complication of post-carotid stenting. The aim was to describe the imaging appearance and discuss its pathophysiology.

Method: This is a retrospective review of patients who underwent mechanical thrombectomy for acute stroke at a single institution over the period of one year. All patients underwent the standard acute stroke imaging protocol (CT head, CT angiogram (CTA) and CT brain perfusion) and when clinically appropriate followed by catheter angiogram and mechanical thrombectomy. ISFT was defined as an arterial luminal filling defect with Hounsfield density equal to or greater than iodine seen on the biplanar CT or conventional CT. The presence and location of ISFT were documented. Standard CT angiogram (CTA) or magnetic resonance angiogram (MRA) was performed 24–48 hours after the neurointerventional procedure to assess for recanalization, volume of infarction and the fate of the ISFT.

Results: ISFTs were identified in eight (five males and three females, age range 18–80 years) out of 49 patients in the following locations: distal M1 ($n = 1$), M2 ($n = 4$), M3 ($n = 1$), A1 ($n = 1$), distal A2 ($n = 1$). ISFT and vessel recanalization occurred in five patients on follow-up. ISFT and vessel occlusion persisted in two patients.

Conclusion: ISFT is likely the result of mechanical disruption of a thromboembolus, and porosity of the thromboembolus fragment may transiently retain iodinated contrast. Recognition of this entity may be important to aid detection of residual thromboembolism and avoid misinterpretation as calcified thromboembolism.

Keywords

CT angiography, iodine-stained fragmented thromboembolism, peri-procedural thrombus fragmentation

Introduction

The recent success of endovascular treatment for acute ischemic stroke has changed clinical practice. Newer generation mechanical thrombectomy devices, such as stent retrievers, have become the standard of care in the management of acute cerebral ischemia in eligible patients. The mechanical action of intra-arterial clot retrieval can occasionally result in peri-procedural thrombus fragmentation (PTF), defined as fragmentation of the parent thrombus leading to distal embolization. Several factors may contribute to thrombus fragmentation including guidewire mechanics, vessel architecture, presence or absence of additional aspiration, and clot composition.[1–4] As endovascular devices and techniques continue to improve and evolve, in combination with improved imaging resolution, there is greater emphasis placed on the recognition of residual fragmented thrombi which can have adverse effects on outcome including increased size of the infarct zone, impaired collateral circulation and overall impedance of clinical outcome. In the immediate aftermath following mechanical thrombectomy, fragmented thrombi may retain iodinated contrast which can be detected on either Dyna-CT Angiography or conventional CT or CTA. The iodine-stained fragmented thromboembolism (ISFT) increases its conspicuity for detection. ISFT is defined as an arterial luminal filling defect with Hounsfield density equal to or greater than the density of iodine within the contralateral vessel. We performed a retrospective review of all cases of mechanical thrombectomy performed in our institution over a period of one year and aimed to analyze the incidence, as well as to describe imaging findings of ISFT

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and to discuss its pathophysiological mechanisms and clinical relevance.

Materials and methods

The ethics review board approved this study. A retrospective review from January 2016 to December 2016 of acute stroke patients undergoing mechanical embolectomy for large proximal intracranial blood vessels occlusion was conducted. Proximal arterial occlusion included those located at the terminal intracranial carotid artery, M1-M2 segment of the middle cerebral artery (MCA) or A1-A2 segment of the anterior cerebral artery (ACA). A total of 49 patients (21 females and 28 males) with a mean age of 63 years (range 18–87 years) were reviewed. All patients underwent the standard acute stroke imaging protocol which included a plain CT head, CTA and CT perfusion performed using a SOMATOM Definition Flash (Siemens Healthcare, Forchheim, Germany) dual energy CT (DECT) scanner. Cerebral catheter angiography and mechanical thrombectomy were performed in a biplanar angiography suite with DynaCT capability (Siemens Artis Q biplane with PURE software). Neurointerventionalists involved in the study utilize the Solumbra technique which encompasses use of a combined stent retriever (Solitaire device) with aspiration technique directly at the thrombus interface. In addition to conventionally acquired intra-procedural digital subtraction angiography (DSA) images, final angiographic runoffs included a 3D-mode acquisition with exposure parameters as follows: voltage 70 kV with no added copper filtration, pulse width 12.5 ms, dose 0.36 μGy/fr, I-noise reduction turned off, edge enhancement NAT 20%, edge enhancement SUB 5%, window center 900, window width 2400, window brightness 3100, window contrast 35, extended pixel width 16, 3D type DSA, 3D auto control, angle 200° and angulation step 1.5°/fr.

Two fellowship-trained staff neuroradiologists (CC-TH and TWW) reviewed each case independently with a final agreement on consensus. Location of the initial site of proximal large intracranial arterial occlusion was documented on either CTA. Immediately after the completion of mechanical thrombectomy a modified thrombolysis in cerebral infarction (TICI) grading score of the affected vascular territory was assigned. ISFTs were identified on either the angiography suite utilizing on-table DynaCT in the immediate aftermath of the thrombectomy procedure or a conventional CT. The density of ISFT was identified qualitatively. In selective cases when the CT scan was obtained at one of our DECT scanners (Siemens SOMATOM Definition Flash or SOMATOM Force), the ISFTs were quantitatively analyzed by placing a region of interest on the ISFT and comparing its density with the iodine density of the contralateral vessel. Finally, CT head, CTA, magnetic resonance imaging (MRI) brain and MRA studies performed 24–48 hours after the index procedure were reviewed to determine the fate of the ISFT and vessel recanalization; an approximation of the acute infarct volume (mL) was calculated using the ABC/2 methodology described by Sims et al.[5]

Results

Out of 49 acute stroke patients who received mechanical thrombectomy, eight patients (male:female = 5:3, mean age 55 years, range 18–80 years) were identified with ISFT (8/49, 16%). In seven of these patients, ISFT was identified by on-table DynaCT immediately following the procedure. ISFTs were located in the distal M1 ($n = 1$), M2 ($n = 4$), M3 ($n = 1$), A1 ($n = 1$) and distal A2 ($n = 1$). In five of the eight patients, the ISFT resolved on follow-up CT head and MRI inside 24–48 hours of mechanical thrombectomy. Persisting ISFT with vessel occlusion was observed in two of the seven patients. One of the eight patients had an ISFT at the distal A2 as a complication post–ipsilateral internal carotid artery stenting and the patient underwent immediate thrombectomy (<1 hour) after the diagnostic CT scan (Figure 1). Final infarct volume had a mean value of 80.5 mL, and range of 3–222 mL. The outlier infarct value of 3 mL corresponds to the carotid stenting patient who underwent timely mechanical embolectomy. Demographic data, site of initial thromboembolic occlusion and location of ISFT of the eight patients are presented in Table 1.

Discussion

In recent medical literature, the incidence of distal embolization from fragmentation of the parent thrombus during mechanical thrombectomy in acute ischemic stroke is reported to vary between 11 and–15%.[6–8] Less than 10% of such fragmented thrombi are of sufficient size (>200 μm) to be angiographically detected, are predominantly in the affected vascular territory due to embolic shower downstream and are less likely to occur in a new vascular territory.[9] Involvement of new vascular territory is usually attributed to reflux of flow, new cardiogenic or artery-to-artery embolism, and inadvertent separation of part of the retrieved thrombus during the retraction phase of mechanical thrombectomy. Smaller-sized distal emboli may spontaneously recanalize during the procedure, especially when intra-procedural thrombolytic agents are administered. Overall, the presence of new distal embolization in the peripheral vasculature is not associated with an unfavorable clinical outcome if the parent vessel is successfully revascularized (modified TICI score ≥ 2).[10] Etiopathogenesis of ISFT is not well understood and is likely multifactorial, but mechanical factors related to the embolectomy procedure and composition of the thromboembolus both play an important role.

Mechanical thrombectomy in the present era utilize a myriad of techniques including contact aspiration, stent retriever with or without proximal balloon

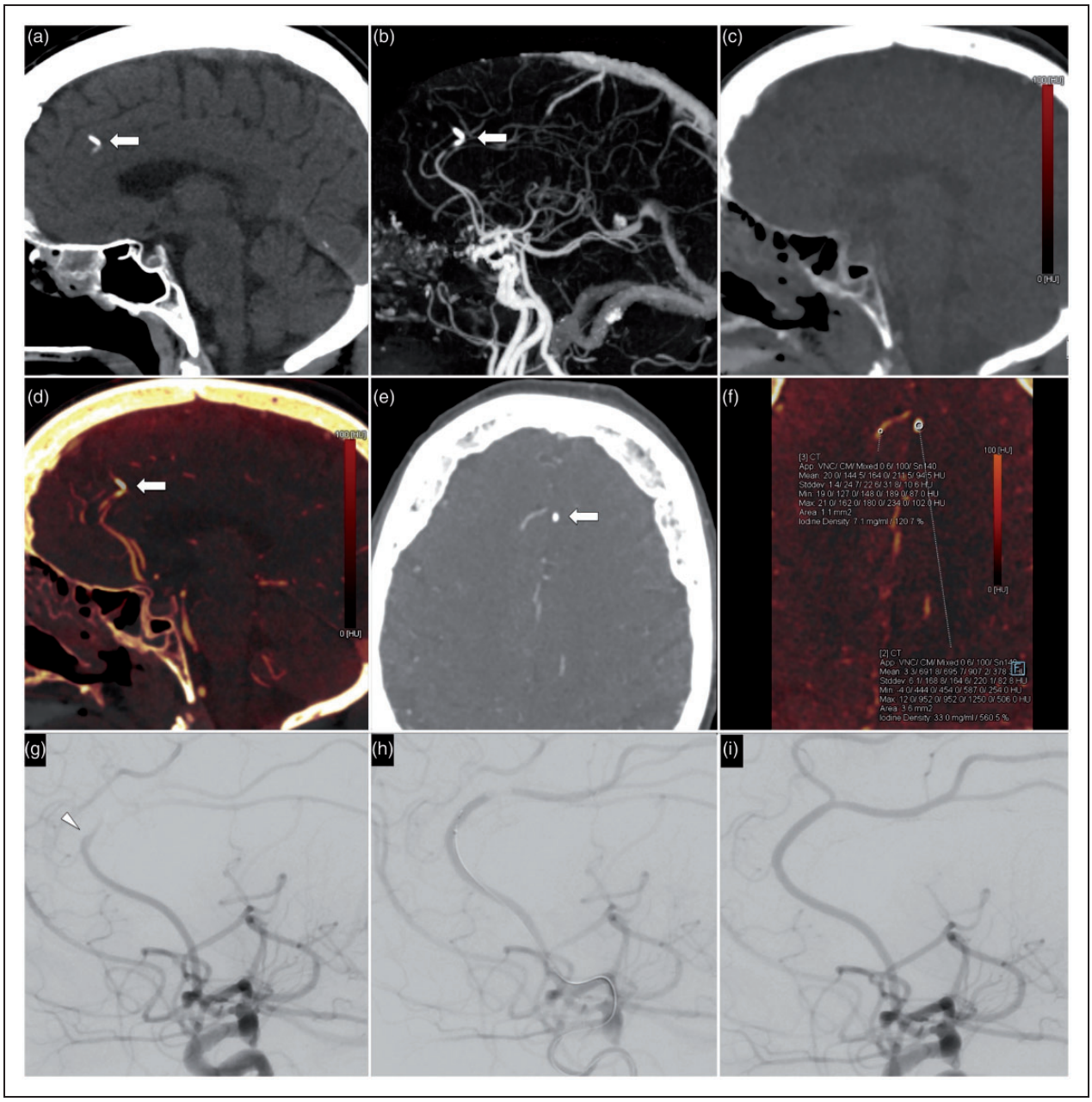

Figure 1. An 80-year-old female with acute left anterior cerebral artery (ACA) territory ischemia immediately following elective left carotid stenting. Plain computed tomography (CT) head (a) showed a hyperdense thromboembolus at the distal A2 of the left ACA (arrow). Dual energy CTA (b to f) acquisition with maximum intensity projection image: (b) confirmed the presence of a hyperdense thromboembolus, virtual non-contrast image; (c) showed subtraction of the thromboembolus favoring the presence of iodine over calcification. Iodine overlay image (d) confirmed increased attenuation of the thromboembolus compared to background iodine in the cerebral vasculature. Axial CTA qualitatively showed the greater attenuation of the thromboembolus compared to the contralateral iodine enhanced vessel. Iodine concentration analysis demonstrated significantly greater iodine density compared to the contralateral enhancing vessel (region of interest (ROI) placed over right ACA 7.1 mg/mL and ROI placed over left thromboembolus 33 mg/mL). Patient proceeded immediately to mechanical thrombectomy. Digital subtraction angiography images (g to i) showed initial occlusion at the distal A2 of left ACA (arrowhead) with subsequent recanalization after deployment of the stent retriever.

inflation, or their combination.[11] In the contact aspiration technique, the thrombus may undergo excessive elongation by negative pressure suction exerted on its proximal surface by the aspiration catheter. The resulting greater surface of interaction between the thrombus and vessel wall predisposes to PTF and this is more pronounced in the presence of tortuous and stenotic vessel architecture.[1,2] In the stent retriever technique, a microcatheter is advanced beyond the thrombus to deploy the stent retriever and, in most instances, additional proximal suction is applied through a balloon guiding catheter to temporarily arrest arterial flow and reduce the pressure gradient across the proximal and distal surfaces of the thrombus.[12,13] Accidental

Table 1. Patient demographics, imaging findings and clinical outcomes.

Case	Age/sex	Clinical history	Site of initial thromboembolic occlusion	Intravenous thrombolysis	TICI score	Location of ISFT	Infarct volume	Outcome
1	80/female	Elective left internal carotid artery stenting. Right hemiparesis and expressive dysphasia immediately post-procedure.	Left distal A2 ACA	No	3	Left distal A2 ACA	3	Successful left A2 mechanical thrombectomy without residual thromboembolism
2	69/male	Acute left MCA stroke	Left M1 MCA	Yes	2B	Left M3 MCA	45	Resolution of ISFT with recanalization on follow-up CT head and MRI 48 hours following the procedure
3	39/female	Acute right MCA stroke	Right M1 MCA	Yes	1	Right distal M1 MCA	140	Persistent ISFT on CT head 24 hours following the procedure
4	69/male	Acute right MCA stroke	Right M1 MCA	Yes	2B	Right M2 MCA	15	Resolution of ISFT and vessel recanalization on follow-up CT head and CTA 24 hours following the procedure
5	18/male	Acute right internal carotid artery dissection with acute right ACA stroke	Right A1 ACA	Yes	1	Right A1 ACA	25	Resolution of ISFT and vessel recanalization on follow-up CT head and CTA 24 hours following the procedure
6	53/male	Acute left MCA stroke	Left M2 MCA	Yes	2A	Left M2 MCA	222	Resolution of ISFT and vessel recanalization on follow-up CT head and CTA 24 hours following the procedure
7	53/female	Acute right MCA stroke	Right M2 MCA	Yes	2A	Right M2 MCA	190	Persistent ISFT on CT head 24 hours following the procedure
8	61/male	Acute right MCA stroke	Right M1 MCA	Yes	2B	Right M2 MCA	4	Resolution of ISFT and vessel recanalization on follow-up CT head and CTA 24 hours following the procedure

ACA: anterior cerebral artery; CT: computed tomography; ISFT: iodine-stained thromboembolism; MCA: middle cerebral artery; MRI: magnetic resonance imaging; TICI: thrombolysis in cerebral infarction.

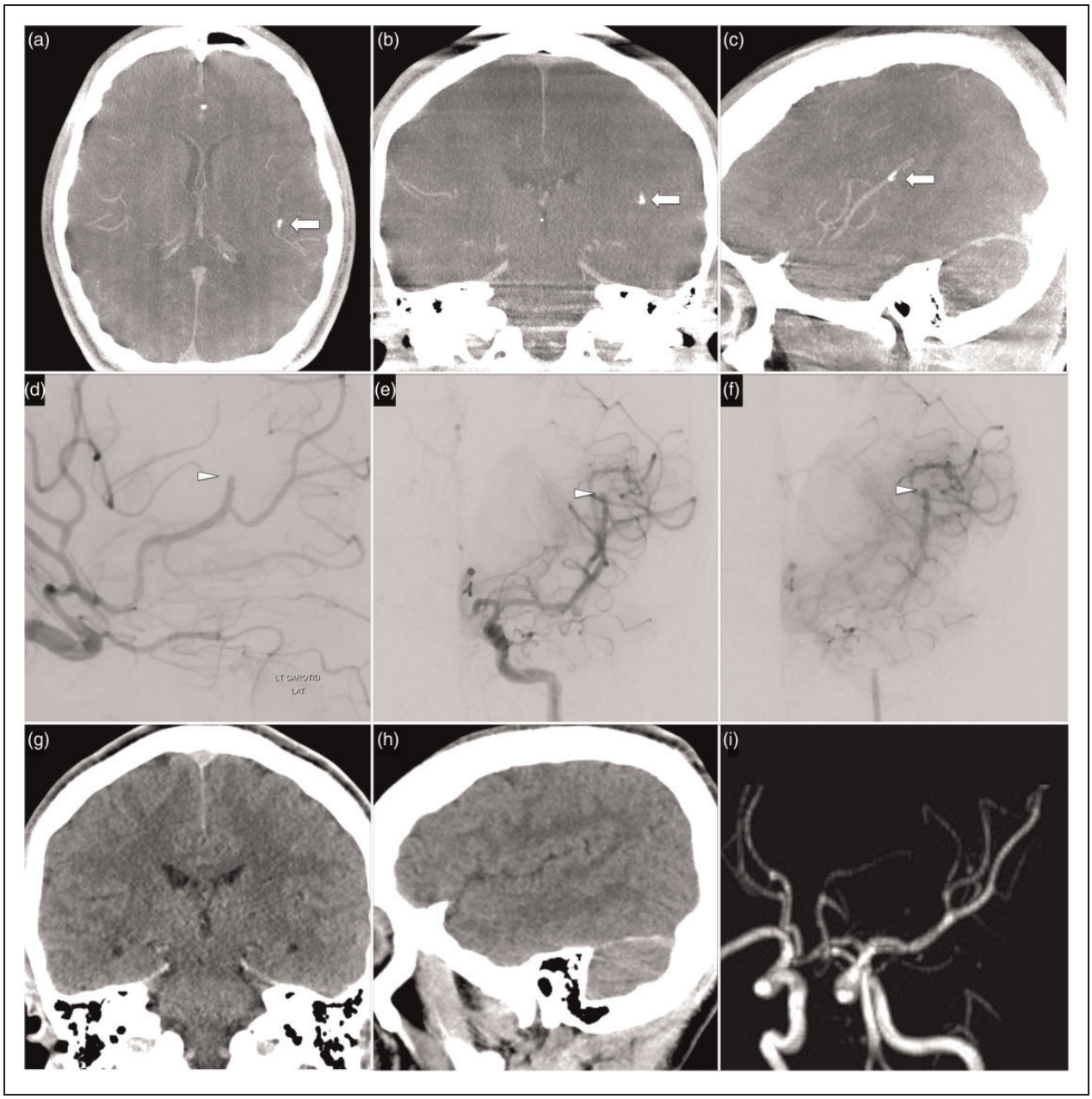

Figure 2. A 69-year-old male with acute left middle cerebral artery (MCA) stroke from occlusion of left M1 MCA. Patient underwent mechanical thrombectomy with residual iodine-stained fragmented thromboembolism (ISFT) seen in the M3 left MCA on the on-table planar computed tomography (CT) (a to c). Digital subtraction angiography showed occlusion of the M3 left MCA with delayed collateral circulation (d to f). Resolution of ISFT on follow-up unenhanced CT head (g and h) and there is complete vessel recanalization on MRA (i) performed 24–48 hours after the procedure.

penetration of the thrombus by the microcatheter or absence of negative pressure suction by the balloon guiding catheter increases the risk of PTF. Combination of both techniques, simultaneously incorporating aspiration catheter and stent retriever, have been described;[14] however, these are not completely immune to the risk of PTF, either. The sudden reduction in the suction force following successful engagement of the thrombus at the tip of the aspiration catheter results in shearing forces causing PTF of the vulnerable elongated thrombus.[2] Interestingly, the majority of PTFs may be sufficiently porous to retain a significant amount of contrast.

Another plausible factor that can contribute to the formation of ISFT is the histological composition of the thrombus. The main constituents of a thrombolus include red blood cells (RBC), fibrin and platelets, in variable proportions.[15,16] Non-cardiogenic thrombus is predominantly RBC-rich (histologically regarded as $> 20\%$ RBC content) surrounded by a thin layer of fibrin and platelets.[3] The viscoelastic properties of RBC, as revealed on direct visualization by scanning electron microscopy, prevent branching of adjacent fibrin monomers, resulting in irreversible disruption to the fibrin cross-linking network and increasing the predisposition to PTF and possibly ISFT.[17] The structural

integrity of the fibrin cross-linking network is fundamental to the stability of the thrombus. In the acute phase of thrombus formation, active cross-linking of adjacent fibrin monomers reduces structural porosity as the thrombus undergoes compaction.[18] The concentration of thrombin is important during this coagulative process as a higher concentration is associated with the establishment of a dense fibrin network of thin diameter strands, whereas a lower concentration results in a loose fibrin network of thick diameter strands.[19] Conversely, cardiogenic thrombi demonstrate a higher resistance against successful mechanical thrombectomy due to their fibrin-rich profile (histologically regarded as $< 20\%$ RBC content), generating a higher coefficient of friction when retrieved; however, their inherent rigidity is protective against PTF.[3,20] Lastly, ISFT may be simply related to PTF and porosity of the clot. An in vivo study has shown that fibrin demonstrated a higher affinity for iodinated contrast than RBC.[21] Despite demonstrating low thrombus density on a non-contrast CT scan, fibrin-rich thrombi markedly increased in density following administration of iodinated contrast, to the extent that a linear positive correlation was reported on a contrast-enhanced spectral detector CT.[21]

ISFT may closely resemble or be observed in conjunction with a contrast column proximal to the fragment on the catheter angiogram or multiphase CTA. This phenomenon is observed when injected iodinated contrast undergoes stasis at the site of vascular occlusion with the absence of collateral circulation, and progressively fades away beyond the late venous phase (Figure 3). This signifies a poor post-thrombolysis recanalization rate.[22] In our case series, ISFT retained contrast for up to 48 hours on a follow-up unenhanced CT following mechanical thrombectomy

In the context of mechanical thrombectomy, the presence of any remaining contrast inside the affected vessel may impede the timely identification of new or residual thrombi on unenhanced CT imaging.[23] In one patient with ISFT following carotid stenting, DECT scanning effectively demonstrated distal embolization containing a high level of iodine contrast (Figure 1). Recent medical literature advocates DECT for detecting residual peripheral intra-arterial thrombus after mechanical thrombectomy.[24] In the immediate post-embolectomy setting, conventional residual thrombus on virtual non-contrast images shows a significantly higher attenuation relative to the perfused arteries but importantly not on the weighted average images (reconstructed conventional image) or iodine map.[23,25] Conversely, ISFT will be of low attenuation on virtual non-contrast images but will show higher attenuation on weighted average images and iodine map.

Despite the described novel findings, the study has several limitations to be considered. Primarily, this is a relatively small case series performed at a single tertiary institution. Additionally, a larger sample size may further explore whether there is a significant correlation between the persistence of ISFT and the subsequent volume of infarction. Nearly all of the patients (7/8) received intravenous thrombolysis prior to the mechanical thrombectomy procedure, which may contribute to increased porosity of the thrombus and also contribute to clearing the thrombus as the majority of the ISFT tend to resolve on follow-up CTA or MRA performed within 24–48 hours after the procedure.

In conclusion, our case series describes ISFT as a subtype of fragmented thrombi following mechanical thrombectomy in acute ischemic stroke. Several factors may cumulatively increase the risk of PTF, and porosity may lead to subsequent uptake of iodinated contrast

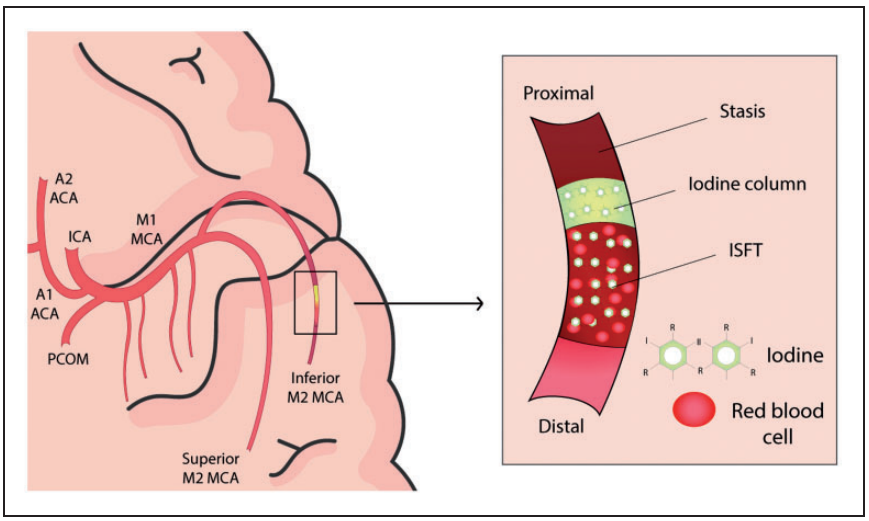

Figure 3. Illustration of an ISFT located in the inferior M2 division of the left MCA with an iodine column immediately proximal to the ISFT followed by stasis of blood flow due to luminal obstruction and impaired collateral circulation. ACA: anterior cerebral artery; ICA: internal carotid artery; ISFT: iodine-stained fragmented thromboembolism; MCA: middle cerebral artery; PCOM: posterior communicating artery.

inside its permeable structure resulting in the detection of ISFT as an arterial luminal filling defect on post-procedural imaging.

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Conflict of interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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