The role of intracoronary thrombolysis in selected patients presenting with ST-elevation myocardial infarction: a case series

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Background
Primary percutaneous coronary intervention (PCI) is the cornerstone of management for ST-elevation myocardial infarction (STEMI). However, large intracoronary thrombus burden complicates up to 70% of STEMI cases. Adjunct therapies described to address intracoronary thrombus include manual and mechanical thrombectomy, use of distal protection device and intracoronary anti-thrombotic therapies.

Case summary
This series demonstrates the use of intracoronary thrombolysis in the setting of large coronary thrombus, bifurcation lesions with vessel size mismatch, diffuse thrombosis without underlying plaque rupture, and improving coronary flow to allow vessel wiring and proceeding to definitive revascularization.

Discussion
Larger intracoronary thrombus burden correlates with greater infarct size, distal embolization, and the associated no-reflow phenomena, and propagates stent thrombosis, with subsequent increase in mortality and major adverse cardiac events. Intracoronary thrombolysis may provide useful adjunct therapy in highly selected STEMI cases to reduce intracoronary thrombus and facilitate revascularization.

Keywords
Case series • Intracoronary thrombolysis • ST-elevation myocardial infarction • Coronary thrombus • Primary percutaneous coronary intervention

Learning points
• Intracoronary thrombolysis may have a role as an adjunct therapy in highly selected cases in the setting of ST-elevation myocardial infarction, particularly with large thrombus burden, to facilitate revascularization.
• This series shows its role in the setting of large coronary thrombus, bifurcation lesions with vessel size mismatch, diffuse thrombosis without underlying plaque rupture and improving coronary flow to allow vessel wiring and proceeding to definitive revascularization.
• Larger intracoronary thrombus burden correlates with greater infarct size, distal embolization and propagates stent thrombosis, with subsequent increase in major adverse cardiac events.

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Introduction

Primary percutaneous coronary intervention (PCI) is the cornerstone of management for ST-elevation myocardial infarction (STEMI). However, large intracoronary thrombus burden complicates up to 70% of STEMI cases. This correlates with larger infarct size, distal embolization with associated no-reflow phenomena, and increases the risk of stent thrombosis, with subsequent increase in mortality and major adverse cardiac events (MACE). Various adjunct techniques have been described including thrombectomy, use of distal protection devices, and intracoronary anti-thrombotic therapies. Adjunct intracoronary thrombolysis (ICT) has been described in cases with failure of thrombus aspiration (TA), large ectatic vessels, and to facilitate PCI in technically difficult lesions. We present a series of four patients with different indications for the use of ICT in the setting of STEMI.

Timeline

| Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|-----------|-----------|-----------|-----------|
| Symptom onset | -4 h | -4 h | -2 | -2 days |
| Triage | 0 h | 0 h | 0 h | 0 h |
| On table | 59 min | 48 min | 31 min | 47 min |
| Thrombus aspiration | N/A | 94 min | 66 min | 77 min |
| Thrombolysis in myocardial infarction grade three | 167 min | 139 min | 68 min | 75 min |
| Intracoronary thrombolysis | 130 min | 161 min | 106 min | 97 min |
| Stent | 183 min | N/A | N/A | 122 min |
| 90-min electrocardiogram | >50% resolution of segment elevation (STE) | >50% resolution of STE with small Q waves | >50% resolution of STE | Partial (50%) resolution of STE, deep Q waves |
| Peak troponin (troponin I, ng/L) | 24 596 at 10 h | 178 833 at 15.5 h | 87 805 at 6.25 h | 98 260 at 13 h |
| Transthoracic echocardiogram | • At 24 h Normal left ventricular (LV) function, left ventricular ejection fraction (LVEF): 68% | • At 14 h Severely impaired systolic function, regional wall motion abnormality, LVEF 10-15%. | • At 24 h Near-normal LV systolic function with mild regional wall motion abnormality | • At 48 h Severely impaired LV systolic function, LVEF 18%. Severe tricuspid regurgitation, moderate severe mitral regurgitation, mild aortic regurgitation |

Case presentations

Patient 1

A 58-year-old man presented with inferior STEMI following 4 h of chest pain, with history of remote paroxysmal atrial fibrillation (AF) in the context of Grave’s thyrotoxicosis (CHA2DS2VASC 0 prior to presentation, not anticoagulated), and current smoker. His vital signs were within normal limits, and he had a normal cardiovascular examination, with ongoing chest pain. He was taken for primary PCI following loading doses of aspirin and prasugrel, in addition to 100 U/kg intra-arterial heparin, and a further bolus dose heparin after 1 h. The culprit lesion was occlusion of a large dominant mid-right coronary artery (RCA) at the level of its bifurcation with a moderate-sized right ventricular branch (Medina 1,1,1) with thrombolysis in myocardial infarction (TIMI) 0 flow in the distal RCA (Figure 1A1,A2). No collaterals were seen from the left system. The lesion could not be crossed despite prolonged attempts and wire escalation using Finecross Microcatheter support with Sion Blue, Pilot 50, Rinato, or Fielder XTR wires. The course of the wire on the lateral aspect of the right ventricle indicated that it was not in the distal RCA. Intracoronary 10 mg Alteplase was administered over 5 min through the guiding catheter, with resultant TIMI 2 flow and small antegrade channel on the first acquisition obtained 8 min after administration of ICT (Figure 1B1,B2). The lesion was crossed with a Fielder XTR wire and sequentially prepared with 1.2 mm and 2 mm semi-compliant and 3 mm non-compliant balloons prior to treatment with a 3 x 20 mm Promus Premier drug-eluting stent, and post-dilatation with a 4 mm non-compliant balloon (Figure 1C, Supplementary material online, Video S1). Peak high-sensitivity troponin levels were reached within 24 596 at 10 h.
10 h of admission at 24 596 ng/L (normal <50 ng/L) following admission value of 35 ng/L and electrocardiogram (ECG) showed resolution of ST-elevation with Q waves present in lead III only (Figure 2). Transthoracic echocardiography (TTE) showed normal left ventricular (LV) function with no regional wall motion abnormalities, and he was discharged on Day 2 of admission on aspirin, prasugrel, and statin therapy. No AF was seen during the admission and CHA 2DS2Vasc score was 1, thus triple therapy was not prescribed.

Patient 2

A 61-year-old man presented with 4 h of generalized malaise, vomiting, and hypotension (blood pressure 80/55 mmHg unsupported) in the context of poorly controlled insulin-dependent type II diabetes mellitus. On evaluation, he had severe hyperglycaemia (blood glucose level >40 mmol/L) with associated hyperosmolar ketosis, mild acidosis with pH 7.31 (normal range 7.35–7.45) and an ECG demonstrating inferolateral ST-elevation, but no signs of cardiac failure on examination. The patient was commenced on insulin/dextrose infusion and loaded with aspirin and prasugrel prior to transfer for angiography, which demonstrated multi-vessel thrombotic disease (complete occlusion proximal RCA, sub-total occlusion left intermediate artery). A 100 U/kg heparin with further bolus dose after 1 h and bailout Abxicimab bolus 0.25 mg/kg were administered. The right coronary artery was initially targeted, with large thrombi aspirated using 6Fr Thrombuster and 6Fr Guideliner systems without restoration of flow (Figure 3A–C). Gentle balloon dilatation along the length of the vessel resulted in transient TIMI 3 flow (Figure 3D), however, the vessel re-occluded, refractory to repeat attempts at TA. ICT was administered with 10 mg Alteplase delivered at the RCA crux using a 6Fr Guideliner over 2 min. The patient developed ventricular standstill which resolved with 600 mcg atropine and 200 mcg adrenaline, with resultant TIMI 3 flow into the entire RCA, postero-lateral (PL-R) and posterior descending artery (PDA-R) branches, revealing an underlying residual 40% smooth stenosis felt unlikely to be the culprit (Figure 3E; Supplementary material online, Video S2). Attention was turned to the left intermediate artery, which developed TIMI 3 flow after single pass TA with 6Fr Thrombuster, and revealing an underlying 30% smooth lesion, again unlikely to represent a thrombotic culprit lesion. Given ongoing significant metabolic derangements and absence of ruptured vulnerable plaque, further PCI was not attempted and the patient was continued on medical therapy with 12 h intravenous Abxiximab infusion in addition to dual antiplatelet therapy, with a transition to intravenous heparin following cessation of Abxicimab. Post-procedure ECG demonstrated >50% improvement of ST segments with marked inferior Q waves (Figure 4). Peak high-sensitivity troponin levels were reached within 17 h of admission at 178 833 ng/L following admission value of 2032 ng/L. Transthoracic echocardiography performed immediately following the procedure demonstrated severe segmental left ventricular dysfunction with an estimated ejection fraction.
between 10–15% and apical left ventricular thrombus. The patient had a protracted admission to the intensive care unit complicated by cardiogenic shock, multi-organ failure, recurrent ventricular tachycardia, suspected gastrointestinal bleed and significant deconditioning with a subsequent decision against further aggressive medical treatment and was admitted to a respite facility.

**Patient 3**

A 65-year-old man presented with a 2-h history of chest pain in the context of inferior STEMI. He was initially hypotensive to systolic blood pressure (SBP) 65 mmHg, which was fluid responsive. He otherwise appeared diaphoretic, however did not have any other clinical features of cardiac failure. His history was significant for prior inferior STEMI in 1997 with angiography following systemic thrombolysis showing intraluminal filling defects in the proximal RCA and PL-R. This was further complicated by scar-mediated ventricular tachycardia requiring secondary prevention internal cardioverter defibrillation, in addition to traditional risk factors including hypertension, type II diabetes, hypercholesterolaemia and previous 40-pack year smoking history. Most recent TTE in 2017 showed LVEF 50% with basal inferior and basal-to-mid inferolateral hypokinesis. He had ceased Aspirin awaiting maxillary sinus surgery. He was taken for primary PCI following administration of loading doses of Aspirin and Ticagrelor, with additional intra-arterial heparin 80 U/kg and bailout Abxicimab bolus 0.25 mg/kg given. The culprit, a large ectatic RCA was occluded distally. Multiple passes at manual TA with 7 Fr Thrombuster and 6 Fr Guideliner into both PDA-R and PL-R branches yielded large thrombi, however with a persistent large burden of residual coronary thrombus shifting between the two branches between aspirations (Figure 5A). A 10 mg Alteplase was delivered to the distal RCA via a Finecross Microcatheter over 5 min, with resultant TIMI 3 flow (Figure 5B). Sequential balloon dilatation with semi-compliant balloons up to 3 mm was performed in the PL-R (Figure 5C Supplementary material online, Video S3), and the patient

**Figure 2** Patient 1 baseline electrocardiogram (A); 90-min following revascularization (B).
was pain-free at the end of the procedure with complete resolution of ST-elevation and unchanged pre-existing Q waves inferiorly (Figure 6). Post-procedurally the patient continued 12 h Abxicimab infusion in addition to ongoing dual antiplatelet therapy. Intravascular ultrasound performed on Day 3 of admission demonstrated fibrocalcific atheromatous plaque in the proximal PL-R with minimal lumen area (MLA) 4.4 mm$^2$ and minor plaque in both distal RCA (with MLA 27 mm$^2$) and PDA-R. Given adequate MLA and significant size mismatch the patient was managed with optimal medical therapy. Peak high-sensitivity troponin levels were reached within 6 h of admission at 87 805 ng/L following admission value of 24 ng/L. Transthoracic echocardiography demonstrated near-normal left ventricular function with hypokinesis in the mid-inferior and apical segments in addition to those described in his previous study. The infarct was likely precipitated by a cessation of all antiplatelet therapy, thus he was discharged on Aspirin and Ticagrelor in addition to ongoing risk factor optimization.

**Patient 4**

A 66-year-old woman presented with inferior STEMI complicated by complete heart block and hypotension following a 2-day history of chest pain. Initially, peripheral pulses were not palpable, with recurrent doses of atropine and fluid resuscitation required to maintain a heart rate of 55/min and SBP of 85 mmHg. She appeared pale, clammy, and unwell, however with no overt signs of cardiac congestion. Her background history included insulin-dependent type II diabetes mellitus and breast cancer in remission previously treated with radiotherapy and ongoing hormone therapy. She was stabilized on an adrenaline infusion and loaded with Aspirin and Prasugrel prior to transfer for angiography. A prophylactic temporary pacing wire was inserted, which was removed on completion of the case. Coronary angiography showed multi-vessel disease, including an occluded mid-RCA (culprit lesion) (Figure 7A), as well as tandem 70% and 80% lesions within the mid-to-distal left anterior descending artery, and long 90% lesions within both first and second obtuse marginal branches. Culprit only PCI was pursued with initial attempts at TA with 6 Fr Thrombuster and 6 Fr Guideliner, as well as balloon dilata
tion with 2.25 mm compliant balloon failing to restore flow beyond the acute margin (Figure 7B). A 10 mg Alteplase was subsequently delivered over five minutes to the mid-RCA via a Finecross Microcatheter, with the restoration of TIMI 2 flow (Figure 7C), following which an exchange was made to a 7 Fr guide system, with further TA with 7 Fr Thrombuster resulting in TIMI 3 flow (Figure 7D). The vessel was then treated with overlapping 2.75 mm $\times$ 28 mm and 2.5 mm $\times$ 38 mm Synergy drug-eluting stents which were post-dilated to 2.75 mm distally and 3 mm proximally with non-compliant balloons (Figure 7E; Supplementary material online, Video S4). Peak high-
**Figure 4** Patient 2 baseline electrocardiogram (A); 90-min following revascularization (B).

**Figure 5** Patient 3 presenting with inferior ST-elevation myocardial infarction, culprit right coronary artery had recurrent large thrombus burden treated with thrombus aspiration, intracoronary thrombolysis, and POBA. (A) Right coronary artery injection with recurrent large thrombus burden despite thrombus aspiration with 7 Fr Thrombuster and 6 Fr Guideliner; (B) right coronary artery immediately following administration of intracoronary thrombolysis; (C) right coronary artery following intracoronary thrombolysis and POBA (final angiographic result). POBA, plain old balloon angioplasty.
sensitivity troponin levels were reached within 13 h of admission at 98 260 ng/L following admission value of 37537 ng/L. Electrocardiogram at 90 min showed only partial resolution of inferior ST-elevation (Figure 8), and TTE performed at 48 h showed severe left ventricular systolic impairment with severe diffuse hypokinesis, LVEF approximately 18%, severe tricuspid, and moderate-severe mitral regurgitation. She was referred for surgical review for consideration of coronary artery bypass grafting and valvular repair; however, due to poor graft targets, comorbidities, and overall frailty was deemed for medical management alone.

**Discussion**

In uncomplicated STEMI, primary PCI is the single most powerful therapy offered by the interventional cardiologist. Concomitant large intracoronary thrombus presents an additional challenge, and confers an increase in mortality and MACE.

Results of ICT in unselected STEMI patients have been mixed. In a randomized controlled trial involving 440 patients with proximal-mid vessel occlusion, intracoronary Alteplase did not reduce microvascular obstruction as measured on contrast magnetic resonance imaging. Conversely, another randomized trial comparing adjunct intracoronary streptokinase with placebo in 95 patients undergoing primary PCI showed improvement in early and late outcomes, including infarct size and LVEF.

Conversely, in selected cases, results are more encouraging. The DISSOLUTION trial randomized 102 patients with STEMI and massive thrombus burden to Urokinase or normal saline, followed by manual aspiration, with the Urokinase arm showing higher rates of TIMI 3 flow, improved ST-segment resolution, and MACE at...
In a series of 34 patients with visible thrombus or distal no reflow, intracoronary Tenecteplase successfully dissolved thrombus or improved flow in 91%. In a registry of 30 patients with large thrombus burden and failed mechanical aspiration, ICT improved TIMI flow in 97%, with only one patient needed repeat revascularization at 14 months follow-up. In 85 patients with previous unsuccessful chronic total occlusion PCI attempt, weight-adjusted Tenecteplase or Alteplase facilitated successful PCI in 54% of patients, with low rates of adverse events.

We have described four difficult cases where vessel patency could not be established or maintained despite guideline-directed pre-treatment with aspirin and either prasugrel or ticagrelor, and escalation of treatment to include TA and bailout GpIIb-IIIa inhibitor (Abciximab used for second and third cases, however no longer available in Australia at the time of the fourth case). Subsequently, ICT with Alteplase was used to facilitate revascularization in all cases. The dose selected was based on the protocol from the T-time trial, with the administration of 10 mg Alteplase directly into the infarct-related artery over 5–10 min. More rapid infusion in one patient resulted in a ventricular standstill, which may have been due to reperfusion; however, drug-related effect remains a possibility, thus subsequent operators continued with the T-time trial protocol. The delivery device chosen was operator dependent.

Conclusion

This series describes ICT in STEMI complicated by high thrombus burden, resulting from vulnerable plaque (Patients 3 and 4) or in a generalized prothrombotic state (Patient 2), and its potential utility to facilitate difficult PCI (Patient 1), where conventional techniques have failed to establish flow. Whilst we do not advocate its routine use, these cases highlight the difficulties in managing intracoronary thrombus, and unique situations in which ICT provides a useful adjunct in complicated STEMI presentations.

Lead author biography

Dr Sumita Barua is a cardiologist, having recently completed cardiology advanced training at Westmead Hospital. Her interests include coronary intervention and advanced heart failure therapies.
Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patients in line with COPE guidelines.

Conflict of interest: none declared.

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