Safety Profile of Intra-Arterial Tirofiban as a Rescue Therapy during Mechanical Thrombectomy in Acute Ischemic Stroke

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Abstract

Purpose This article studies the safety profile and role of intra-arterial (IA) tirofiban as a rescue therapy in acute ischemic stroke (AIS) patients undergoing mechanical thrombectomy.

Methods This is a retrospective observational study conducted among AIS patients with large vessel occlusion (LVO) eligible for endovascular revascularization and in whom IA tirofiban is given as rescue therapy. If the target vessel shows reocclusion following initial recanalization, flow limiting or significant residual stenosis after thrombectomy, or requires balloon angioplasty or stenting, IA tirofiban at a dose of 0.4 µg/kg/min was administered through the microcatheter in the target vessel followed by intravenous infusion of 0.1 µg/kg/min. The primary safety measure of the study was the incidence of symptomatic hemorrhage.

Results The total number of patients in the study group was 82, 36 were in the tirofiban group and 46 were in the non-tirofiban group. Immediate successful reperfusion was achieved in 31 patients (86.1%) and 41 patients (89%) in the tirofiban and non-tirofiban groups, respectively. Note that 19.4 and 25% of patients in the tirofiban group required adjunct techniques of angioplasty and stenting, respectively. Also, 2.7% patient in the tirofiban group had a symptomatic hemorrhage, while 8.7% in the non-tirofiban group had symptomatic intracranial hemorrhage. On multinomial logistic regression, history of transient ischemic attack, truncal occlusion and watershed infarct pattern predicted the usage of IA tirofiban during mechanical thrombectomy.

Conclusion Usage of IA tirofiban with or without adjunct techniques as a rescue therapy during mechanical thrombectomy in LVO improved recanalization rates without increasing the risk of symptomatic hemorrhage.

Keywords
- mechanical thrombectomy
- rescue therapy
- tirofiban

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Introduction

Stroke is an important cause of morbidity and disability affecting the productive life of an individual with substantial socioeconomic impact.[1] Acute ischemic stroke (AIS) due to large vessel occlusion (LVO) can be in situ occlusion due to underlying intracranial atherosclerotic disease (ICAD) or thromboembolism (cardiac-embolism/artery-to-artery embolism). Recanalizing the acutely occluded vessel as early as possible is the strongest predictor of good clinical outcomes. Since 2015, mechanical thrombectomy (MT) has become the standard of care in acute LVO in appropriately selected patients based on the results of five randomized control trials.[2,3] The period for mechanical clot removal was extended up to 24 to 48 hours in patients with small infarct core and large penumbra based on the DAWN and DEFUSE 3 trials.[4,5] However, failure of recanalization has been reported variably between 13.8 and 27.6% of the treated cases,[3,6,7] adversely affecting the favorable functional outcome.[8–10] There are no established guidelines for rescue therapy in the event of unsuccessful recanalization during MT. MT can cause endothelial damage and plaque disruption resulting in subsequent platelet activation and occlusion of the initially recanalized vessel. Tirofiban is approved for use in acute coronary syndrome by the U.S. Food and Drug Administration, a short-acting inhibitor of the glycoprotein IIb/IIIa receptor (GpIIb/IIIa).[11] Tirofiban blocks platelet aggregation and subsequent thrombus formation. Low-dose intra-arterial (IA) tirofiban was tried as a rescue therapy following MT in AIS in a few observational studies.[12–16] Its specific nature of inhibition on ongoing platelet aggregation and thrombus formation with high affinity for GpIIb/IIIA receptor and a short duration of action seemed to be a potential and safe tool in treating AIS.[17] IA administration reduces the drug dosage and increases the local drug concentration, thereby reducing the risks of systemic bleeding. However, the safety and efficacy of IA tirofiban are not well established in acute stroke thrombectomy, with no studies on the Indian population.

Materials and Methods

The study was conducted in the Department of Interventional Radiology, Kovai Medical Center and Hospital, Coimbatore, Tamil Nadu, India, after approval by the local ethical and scientific committee.

Patient Selection

A retrospective review of 82 patients who were 18 or older diagnosed with AIS due to LVO in anterior or posterior cerebral circulation and those who underwent endovascular MT between June 2019 and June 2021 was done. All patients' relevant clinical, demographic, imaging, angiography, and procedural data were collected. Hospital Information System and Picture Archiving and Communication Systems were used to manage patient details. Among the 82 patients, 36 patients received tirofiban during MT.

Baseline Assessment

Essential clinical examination was done to assess the severity of the stroke. All the patients with suspected stroke underwent imaging (computed tomography [CT]/magnetic resonance imaging [MRI]) to exclude intracranial hemorrhage (ICH) and to look for LVO. Clinical severity and imaging parameters were used to select the patient's eligibility for MT per the American Heart Association/American Stroke Association guidelines.[2]

Endovascular Procedure

Intravenous thrombolysis was avoided in eligible patients if he/she can be shifted for MT without delay. Eligible patients underwent MT of the target vessel using suction, stent retriever, or a combination of both as an initial approach. Modified Thrombolysis in Cerebral Infarction (mTICI) score was used to grade the recanalization following thrombectomy. IA tirofiban bolus was administered as a rescue therapy followed by intravenous injection if there is target artery reocclusion following initial recanalization, residual stenosis after thrombectomy ($>$ 30%) preventing effective reperfusion, flow limiting intimal injury causing recurrent thrombus formation, and before balloon angioplasty or stenting. IA tirofiban at a dose of 0.4 µg/kg/min was administered through the microcatheter in the target vessel followed by intravenous infusion of 0.1 µg/kg/min. Tirofiban was not administered if the patient had no recanalization of target vessel after three attempts of MT, history of intracerebral bleeding within 30 days, active bleeding or bleeding tendency, major surgery or severe cranial trauma within 1 month, history of thrombocytopenia with prior exposure to glycoprotein inhibitor, or evidence of hypersensitivity to tirofiban.

An intravenous infusion was continued postprocedure for 6 hours and was overlapped with an oral antiplatelet (loading dose of 300 mg of aspirin) after ruling out ICH. An intravenous infusion was not administered if there was no recanalization of the parent vessel following the IA bolus. Also, intravenous tirofiban infusion was discontinued if the postprocedure MRI (susceptibility-weighted imaging [SWI] sequence) showed evidence of hemorrhage ($>$ HI1). Angiographic outcomes following tirofiban infusion were documented. In the presence of significant residual stenosis ($>$ 70%) following MT, balloon angioplasty/stenting of the target vessel was done in appropriate clinical situations. General anesthesia was preferred if the patient had a posterior circulation stroke, was uncooperative for the procedure, or required intracranial angioplasty or stenting. All other patients had thrombectomy under local anesthesia and conscious sedation.

Postprocedure Evaluation

Immediate postprocedural CT and MRI were taken to look for ICH and postprocedure changes to guide further clinical management. Repeat CT was performed within 24 to 48 hours of the procedure or whenever clinical symptoms suspected an intracerebral hemorrhage. The Heidelberg Bleeding Classification was used to classify ICH. Symptomatic ICH (sICH) was defined as hemorrhage on CT and

Table 1 Baseline characteristics between two patient groups

Characteristics	With IA tirofiban ($n = 36$)	Without IA tirofiban ($n = 46$)	*p*-Value
Age, mean (SD)	56.14 (14.55)	56.46 (12.34)	0.457
Male (%)	21 (58.4)	32 (61.6)	0.291
Female (%)	15 (41.6)	14 (30.4)	0.291
Diabetes mellitus (%)	17 (47.2)	17 (36.9)	0.349
Hypertension (%)	15 (41.7)	16 (34.8)	0.523
Cardiac ailment (%)	3 (8.3)	21 (45.7)	**< 0.001**
H/o Transient ischemic attack (%)	8 (22.2)	1 (2.2)	**< 0.004**
H/o antiplatelet use (%)	1 (2.8)	6 (13)	**0.014**
Dyslipidemia (%)	18 (50)	24 (52.2)	0.845
SBP on arrival, mean mm Hg (SD)	143.89 (24.29)	136.30 (23.79)	0.198
DBP on arrival, mean mm Hg (SD)	87.51 (16.10)	80.22 (11.64)	0.022
RBS on arrival, mg/dL (SD)	156.81 (77.90)	156.74 (75.31)	0.948
HbA1c, mean	6.98 (2.22)	6.75 (2.16)	0.273
LDL, mean mg/dL (SD)	103.03 (38.43)	107.3 (28.87)	0.617
NIHSS, median (IQR)	18.5 (13–21)	16.5 (14–22)	0.188
ASPECTS, mean (SD)	7.1 (1.47)	6.76 (1.67)	0.388
Pc ASPECTS, mean (SD)	6.1 (1.34)	8.33 (1.54)	**0.033**
Onset to arrival, mean min (SD)	295.79 (478.39)	205.35 (190.96)	0.123
IV thrombolysis	2 (5.6)	7 (15.2)	0.165
Location of LVO			
Supraclinoid ICA	2	0	
ICA terminus	5	14	
M1 MCA	17	21	
M2 MCA	2	5	
A1 ACA	0	1	
V4 vertebral	3	1	
Vertebrobasilar junction	2	0	
Proximal basilar	2	1	
Mid basilar	2	0	
Basilar top	1	3	
Tandem occlusion	4 (11.1)	7 (15.2)	0.588
Pattern of intracranial occlusion			**< 0.001**
Truncal (%)	21 (58.3)	3 (6.5)	
Branching (%)	15 (41.6)	43 (93.4)	
SWI clot sign	24 (66.7)	38 (82.6)	0.095
Door to image time (SD)	32.78 (14.22)	28.57 (16.36)	0.076
Door to puncture time (SD)	91.22 (34.27)	87.7 (48.78)	0.195
Puncture to recanalization time (SD)	50.54 (23.77)	42.27 (27.59)	**0.049**
Door to recanalization time (SD)	140.36 (41.80)	128.13 (63.09)	**0.159**
Type of mechanical thrombectomy			**0.034**
Solumbra	28 (77.8)	24 (52.2)	
Suction	2 (5.6)	11 (23.9)	
Stent retriever	1 (2.8)	0	
Combination	5 (13.8)	11 (23.9)	

(*Continued*)

Table 1 (*Continued*)

Characteristics	With IA tirofiban ($n = 36$)	Without IA tirofiban ($n = 46$)	*p*-Value
Number of attempts (median)	2	1	0.137
mTICI > 2a (successful reperfusion, %)	31 (86.1)	41 (89.1)	0.678
First pass effect (%)	15 (41.6)	28 (60.8)	0.083
Rescue therapies (%)		NA	**NA**
Tirofiban only	20 (55.5)		
Tirofiban + Angioplasty	7 (19.4)		
Tirofiban + Stenting	9 (25)		
Extracranial angioplasty or stent placement (%)	10 (27.8)	3 (6.5)	**0.008**
Intracranial angioplasty or stent placement (%)	14 (38.9)	0	**< 0.001**
Conscious sedation (%)	16 (44.4)	34 (73.9)	0.007
General anesthesia	20 (55.6)	12 (26.1)	0.007

Abbreviations: ACA, anterior cerebral artery; ASPECTS, Alberta Stroke Program Early Computed Tomography Score; DBP, diastolic blood pressure; HbA1c, glycosylated hemoglobin; IA, intra-arterial; ICA, internal carotid artery; IQR, interquartile range; IV, intravenous; LDL, low-density lipoprotein; LVO, large vessel occlusion; MCA, middle cerebral artery; mTICI, modified Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale; Pc, posterior circulation; RBS, random blood sugar; SBP, systolic blood pressure; SD, standard deviation; SWI, susceptibility-weighted imaging.
The *p*-Values in bold are statistically significant.

neurological deterioration of $\geq$ 4 points on the National Institutes of Health Stroke Scale (NIHSS) score attributable to the bleeding.

Data Analysis

Baseline characteristics and demographics of patients who received IA tirofiban as a rescue therapy during MT were studied. Angiographic improvement following IA tirofiban as a rescue therapy was studied by mTICI score. sICH following IA tirofiban was taken as a measure of safety. Clinical outcomes and modified Rankin Scale (mRS) of patients at 3 months were studied through clinical visits or telephonic interviews wherever possible. Various parameters were compared between the tirofiban and non-tirofiban groups.

Statistical Analysis

Statistical analysis was done using SPSS software. Continuous variables were presented as mean or median and categorical variables were presented as frequencies. The Student's *t*-test or chi-square test was performed to detect significant differences between groups wherever applicable. A *p*-value of < 0.05 was considered statistically significant. Logistic regression analysis was done to see the strength of the association between tirofiban use and relevant categorical variables wherever applicable.

Results

Baseline Characteristics

The total number of patients in the study group was 82, out of which 36 received tirofiban during MT and 46 did not require tirofiban. The mean age was 56.14 ± 14.55 and 56.46 ± 12.34 among the participants with and without tirofiban, respectively. Males formed the predominant gender among subjects in both the tirofiban (69.7%) and non-tirofiban groups (58.4%). Baseline characteristics between the two groups are shown in ►**Table 1**. Diabetes mellitus, hypertension, and dyslipidemia were the most common risk factors in both groups. Random blood sugar at the time of onset of stroke, glycosylated hemoglobin (HbA1c), and low-density lipoprotein (LDL) were comparable between the two groups. The median NIHSS score was slightly higher among those with IA tirofiban. History of transient ischemic attacks (TIAs) was significantly higher among those with IA tirofiban, while cardiac ailment was considerably higher among those without IA tirofiban. Logistic regression analysis showed an odds ratio of 12.85 for TIA and 0.108 for underlying cardiac ailments indicating that patients with a history of TIA are more likely to receive tirofiban by odds of 12 times. The proportion of posterior circulation LVO was slightly higher in the tirofiban group. The truncal pattern of occlusion, defined as occlusion of a midsegment of the vessel not extending to bifurcation, was significantly higher in patients in the tirofiban group (58.3% vs. 6.5%). The branching pattern of occlusion, defined as occlusion extending to a branching point, was significantly higher in the non-tirofiban group (41.6% vs. 93.4%). Background acute or chronic watershed infarcts were more commonly seen in patients in the tirofiban group. Susceptibility vessel sign, as characterized by the blooming artifact in the target vessel, which exceeded the size of the contralateral arterial diameter in SWI MRI and analogous to hyperdense sign in CT, was more common in the non-tirofiban group as compared with the tirofiban group although not statistically significant (82.6% vs. 66.7%, $p = 0.09$). These findings correlate with the presence of ICAD in a majority of patients in the tirofiban group (26 out of 36 patients, 72%). On multinomial logistic regression as represented in ►**Table 2**, TIA, truncal pattern of occlusion,

Table 2 Multinomial logistic regression

Serial no.	Variable	OR	CI	*p*-Value
1	Transient ischemic attack			0.019
	Yes	12.85	1.52–108.37	
	No	1	–	
2	Cardiac ailment			0.001
	Yes	0.108	0.029–0.404	
	No	1	–	
3	Branching			0.000
	Truncal occlusion	1	–	
	Branch occlusion	0.050	0.013–0.191	
4	Watershed infarct			0.003
	Present	11.0	2.27–53.26	
	Absent	1	–	
5	Anesthesia			0.008
	General anesthesia	1	–	
	Conscious sedation	0.28	0.11–0.71	

Abbreviations: CI, confidence interval; OR, odds ratio.

and presence of watershed infarct was significantly associated with usage of tirofiban as a rescue therapy during MT. These patients had higher chances of requirement of general anesthesia during MT due to longer procedure time, higher number of posterior circulation strokes, requirement of intracranial angioplasty, and stenting in uncooperative patients.

Efficacy and Safety of Tirofiban

After initial suboptimal recanalization, successful reperfusion defined as mTICI > 2a was achieved in 31 patients (86.1%) in the tirofiban group following rescue therapy. In the non-tirofiban group, successful reperfusion was achieved in 41 patients (89%) without rescue therapy. After IA tirofiban as initial rescue therapy, angioplasty was required in 15 patients and stenting was needed in 9 patients in the tirofiban group. On assessing the efficiency of IA tirofiban, postprocedure patency of target vessel with > mTICI 2a flow was seen at 86.1% (31 out of 36 patients). In comparison, overall patency was 76.5% (26 out of 36 patients) due to delayed reocclusion of the target vessel in 5 patients in 24 to 48 hours. It represents that adding tirofiban as a rescue therapy improved recanalization in 30% of patients (26 out of 82).

Table 3 Heidelberg reperfusion hemorrhage among the study participants

Serial no.	Variable	IA tirofiban		*p*-Value
		With ($N = 36$) (%)	Without ($N = 46$) (%)	
1	No hemorrhage (0)	28 (77.8)	25 (54.3)	0.298
2	Scattered small petechiae, no mass effect (1a, HI1)	3 (8.3)	6 (13.1)	
3	Confluent petechiae, no mass effect (1b, HI 2)	4 (11.1)	6 (13.1)	
4	Hematoma within infarcted tissue, occupying < 30%, no substantive mass effect (1c, PH1)	0	2 (4.3)	
5	Hematoma occupying 30% or more of the infarcted tissue, with noticeable mass effect (2, PH 2)	1 (2.8)	4 (8.7)	
6	Subarachnoid hemorrhage (3c)	0	2 (4.3)	
7	Subarachnoid hemorrhage (3c) + Confluent petechiae, no mass effect (1b, HI2)	0	1 (2.2)	

Abbreviation: IA, intra-arterial.

Table 4 Safety measures and functional outcomes at 90 days between two groups

Characteristics	With IA tirofiban	Without IA tirofiban	*p*-Value
Any ICH	8 (22.2)	21 (45.7)	**0.027**
sICH	1 (2.7)	4 (8.7)	0.127
mRS 0–2	18 (50)	31 (67.4)	0.087
mRS 6	10 (27.7)	5 (10.8)	**0.049**

Abbreviations: IA, intra-arterial; ICH, intracranial hemorrhage; mRS, modified Rankin Scale; sICH, symptomatic ICH.
The *p*-Values in bold are statistically significant.

Overall hemorrhage following MT was 22.2 and 45.7% of those with and without IA tirofiban, respectively. As per the Heidelberg classification, the predominant hemorrhage pattern in both groups was HI2. Symptomatic hemorrhage was seen among 8.7% of the non-tirofiban group and 2.7% of the tirofiban group as shown in ►**Table 3**. The safety and functional outcomes of patients in both groups are represented in ►**Table 4**. Cases series representing the usage of rescue therapy during MT are illustrated in ►**Figs. 1**–**4**.

Discussion

Tirofiban is a selective GpIIb/IIIa receptor inhibitor. Because of its short half-life and rapid elimination after the cessation of infusion, it is commonly used as a rescue therapy in percutaneous coronary intervention in the event of a thrombotic complication. Because of the inherent risk of hemorrhagic transformation of the infarct in AIS, the safety of GpIIb/IIIa inhibitors is yet to be established as a rescue therapy after thrombectomy. This study assessed the safety

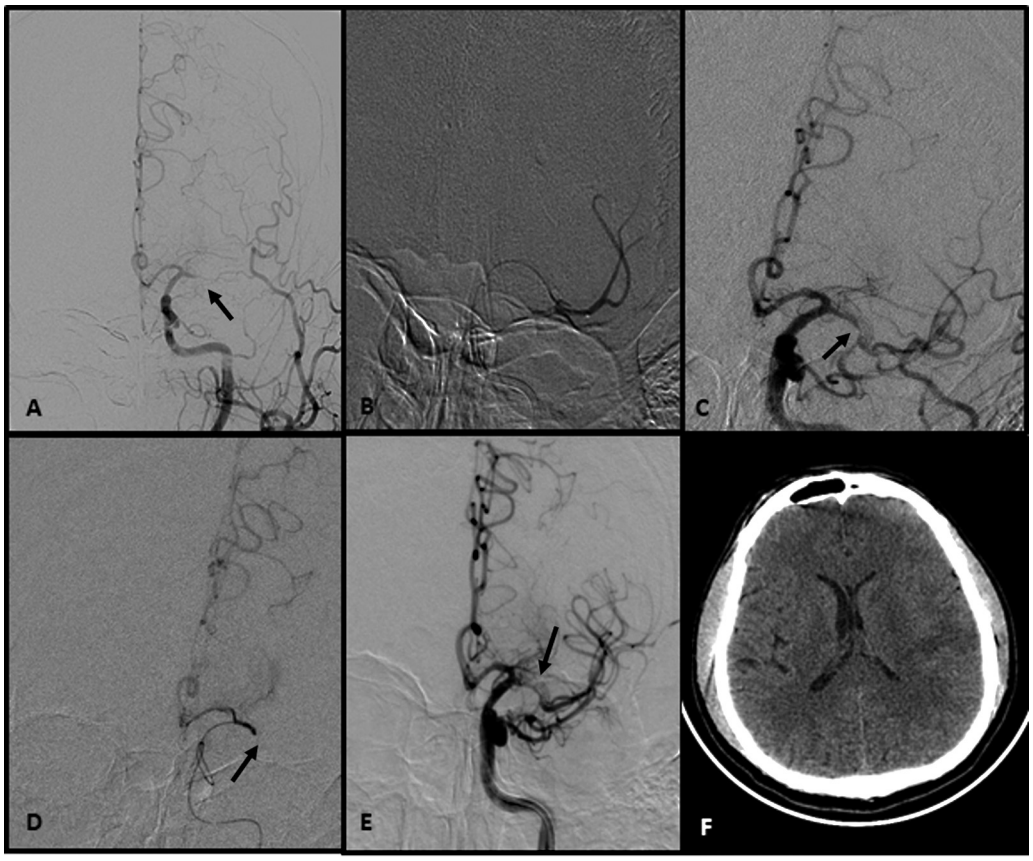

Fig. 1 A 45 years old male, a known diabetic and smoker, presented with right hemiplegia and aphasia for 7.5 hours with National Institutes of Health Stroke Scale (NIHSS) of 15. Imaging showed left M1 middle cerebral artery (MCA) occlusion with diffusion-weighted imaging (DWI) Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of 8. (**A**) (arrow) Left M1 MCA occlusion. He underwent mechanical thrombectomy (**B**) using modified Solumbra technique achieving modified Thrombolysis in Cerebral Infarction (mTICI) 3 recanalization with underlying significant luminal stenosis in the left mid-M1 MCA (arrow, **C**). Check angiogram after a few minutes showing reocclusion of the target vessel (arrow, **D**). The second attempt of mechanical thrombectomy was made, and intra-arterial tirofiban was administered with resultant mTICI 3 flow without further reocclusion (arrow, **E**). Twenty-four hours' follow-up computed tomography (CT) showed no evidence of hemorrhage (F). The patient was functionally independent with a modified Rankin Scale (mRS) score of 1 at 3 months' follow-up.

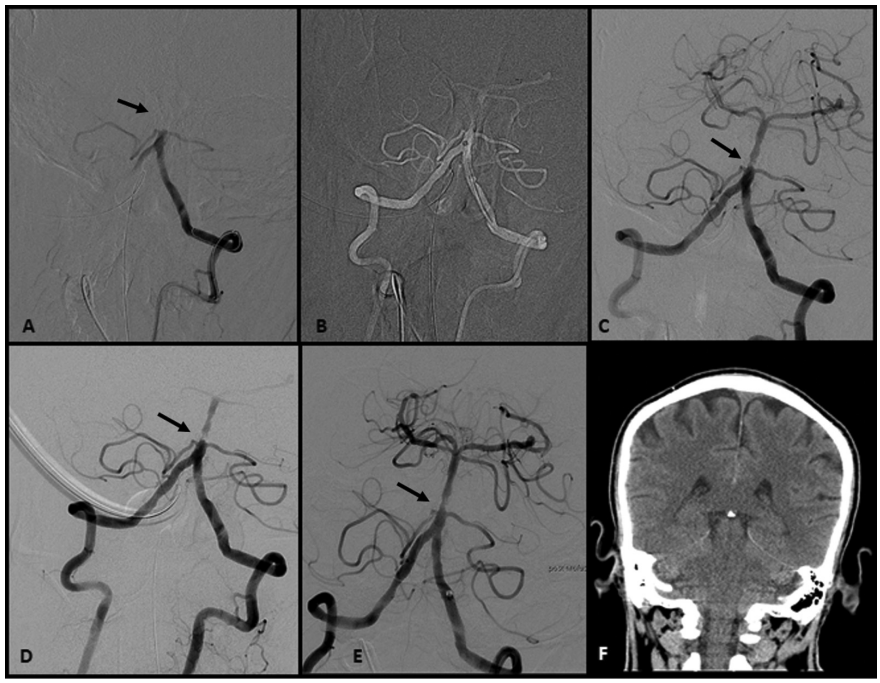

Fig. 2 A 59 years old male, a known diabetic presented with left hemiparesis and slurring of speech on wake up with National Institutes of Health Stroke Scale (NIHSS) of 11. Imaging showed mid basilar occlusion with diffusion-weighted imaging (DWI) posterior circulation Alberta Stroke Program Early Computed Tomography Score (Pc-ASPECTS) of 8. (**A**) (arrow) Mid basilar artery occlusion for which underwent mechanical thrombectomy (**B**) using modified Solumbra technique achieving modified Thrombolysis in Cerebral Infarction (mTICI) 3 recanalization with underlying residual stenosis (arrow, **C**). Check angiogram after a few minutes showing new thrombi formation with slowing of forward flow and impending reocclusion (arrow, **D**). Intra-arterial tirofiban was administered, resulting in improvement of luminal caliber with the good forward flow (arrow, **E**). Twenty-four hours' follow-up computed tomography (CT) showed no evidence of hemorrhage (**F**). The patient was functionally independent with a modified Rankin Scale (mRS) score of 1 at 3 months' follow-up.

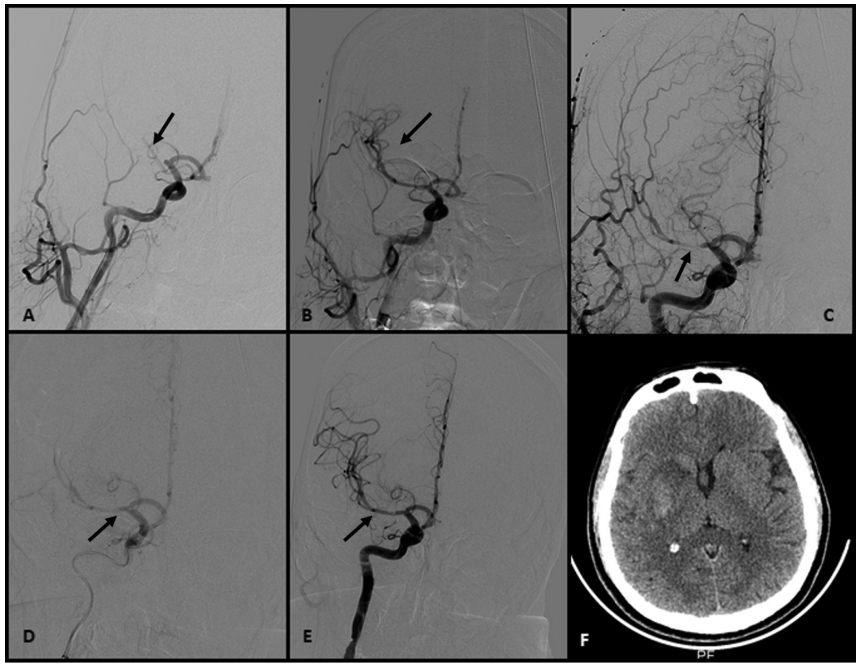

Fig. 3 A 36 years old male, presented with left hemiplegia for 40 minutes with National Institutes of Health Stroke Scale (NIHSS) of 13. Imaging showed right M1 middle cerebral artery (MCA) occlusion with diffusion-weighted imaging (DWI) Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of 7. (**A**) (arrow) Right M1 MCA occlusion for which underwent mechanical thrombectomy using modified Solumbra technique achieving modified Thrombolysis in Cerebral Infarction (mTICI) 3 recanalization (**B**). Check angiogram after a few minutes showing impending reocclusion of the target vessel with slowing of forward flow (arrow, **C**). Intra-arterial tirofiban was administered using a microcatheter (arrow, **D**) resulting in improvement of luminal caliber and mTICI 3 reperfusion without further reocclusion (**E**). Twenty-four hours' follow-up computed tomography (CT) showed asymptomatic HI2 changes, which remained stable. (**F**) The patient was functionally independent with a modified Rankin Scale (mRS) score of 2 at 3 months' follow-up.

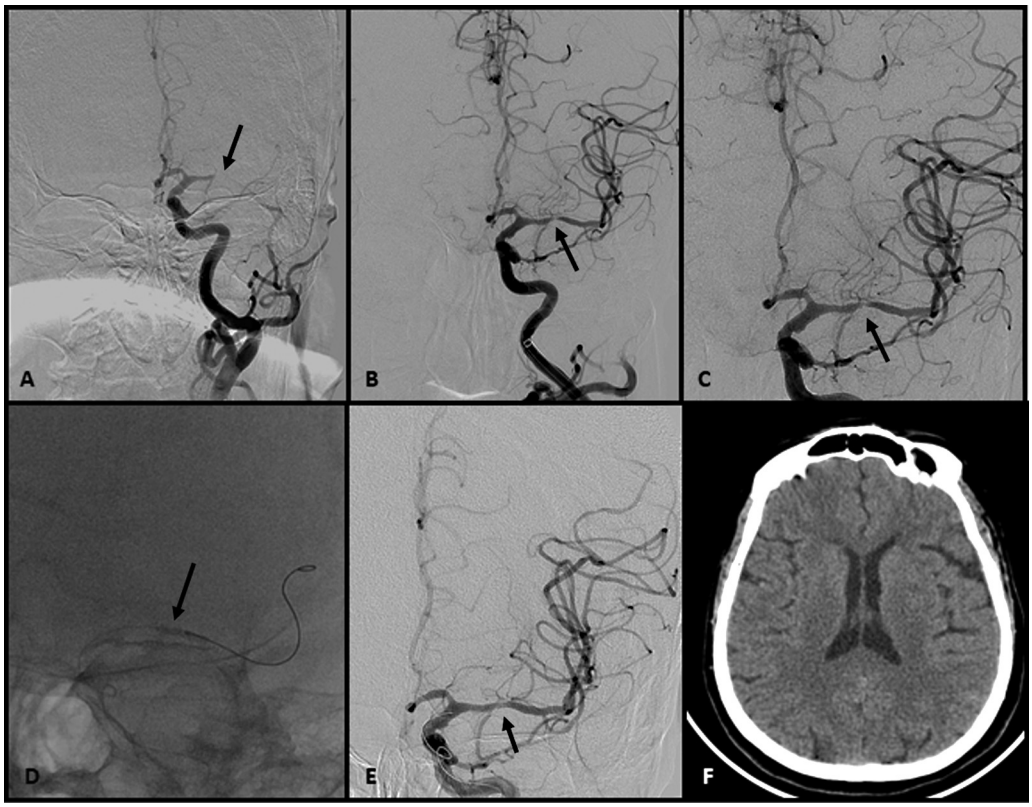

Fig. 4 A 73 years old female who is a known hypertensive presented with right hemiplegia and aphasia for 6.5 hours with National Institutes of Health Stroke Scale (NIHSS) of 20. Imaging showed left M1 middle cerebral artery (MCA) occlusion with diffusion-weighted imaging (DWI) Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of 8. (**A**) (arrow) Left M1 MCA occlusion for which underwent mechanical thrombectomy using modified Solumbra technique achieving modified Thrombolysis in Cerebral Infarction (mTICI) 3 recanalization with significant residual stenosis (90%) (arrow, **B**). Intra-arterial tirofiban was administered using a microcatheter to prevent reocclusion (arrow, **C**). Because of significant residual stenosis due to underlying intracranial atherosclerotic disease (ICAD), submaximal angioplasty of the stenosis of left M1 MCA was done (**D**), achieving good luminal caliber and mTICI 3 reperfusion (arrow, **E**). Twenty-four hours' follow-up computed tomography (CT) showing no evidence of hemorrhage. (**F**). The patient was functionally independent with a modified Rankin Scale (mRS) score of 0 at 3 months' follow-up.

and efficacy of IA tirofiban as a rescue therapy during MT in AIS patients.

Our study population was comparatively younger than in the Western literature. This could be attributed to stroke affecting a relatively younger population in India compared with developed countries.[18] Diabetes mellitus, hypertension, dyslipidemia, random blood sugar, HbA1C, and mean LDL level were equally prevalent in both groups and comparable with the other studies.[19]

We observed that most patients requiring tirofiban have an underlying ICAD and those in the other group predominantly had a cardioembolic stroke. Hence, history of TIAs, LVO showing preference for sites of ICAD (supraclinoid ICA, V4 segment of the vertebral artery, vertebrobasilar junction, and proximal basilar artery), greater time to recanalization, truncal pattern of occlusion, background or active watershed infarcts, and a negative susceptibility vessel sign were reported in the tirofiban group, whereas the non-tirofiban group had a higher prevalence of cardiac ailments, concurring with existing evidence.[13,19–26] Also, the presence of these findings helps to preoperatively predict the possibility of the requirement of tirofiban as a rescue therapy and adjunct angioplasty or stent placement if required during MT. Also, these parameters help in early initiation of tirofiban prior to the first pass through the suction catheter which may help to decrease the number of attempts thereby improving the recanalization rates and time.

Tirofiban was used in 36 (43.9%) out of 82 patients. Successful reperfusion (mTICI 2b, 2c, and 3) was achieved in 31 patients in the tirofiban group (86.1%) and 41 patients in the non-tirofiban group (89%), which were comparable with other studies reported in the literature (►**Table 5**). IA tirofiban was used as a stand-alone rescue therapy in 20 patients (55.5%) in the tirofiban group. Adjuvant extracranial angioplasty or stenting and intracranial angioplasty or stenting were required in 27.7 and 38.8%, respectively, comparable with the literature.[19]

Total hemorrhagic events (asymptomatic and symptomatic) were 35%, with total symptomatic hemorrhage contributing to 6.2% in our study group, similar to published data on the incidence of sICH (4.4%) in the intervention arm on pooled data from five randomized trials by HERMES collaborators.[3] The predominant hemorrhage pattern was HI2, as per the Heidelberg classification in both groups. Note that

Table 5 Summary of past literature reviewing the safety and efficacy of IA tirofiban

Serial no.	Study	Group	ICH	sICH	Mortality	mTICI $\geq$ 2b	mRS 0–2
1	Present study	With tirofiban	22.2	0	30.5	86.1	50
		Without tirofiban	45.7	8.7	10.9	89.1	67.4
2	Kellert et al[28]	With tirofiban	18	16	30	87.5	14
		Without tirofiban	8.9	8	26.8	72.1	26.8
3	Zhao et al[23]	With tirofiban	36.7	11.1	22.2	78.9	45.6
		Without tirofiban	33.3	10	33.3	86.7	36.7
4	Lee et al[29]	With tirofiban	20	8.3	–	90	61.7
		Without tirofiban	20	5.9	–	76.3	48.9
5	Wu et al[30]	With tirofiban	38.3	14.6	29.8	92.4	37
		Without tirofiban	9.7	5.6	21.8	91.1	42.6
6	Yu et al[31]	With tirofiban	19.2	11.5	3.8	88.5	34.6
		Without tirofiban	28.6	14.3	10.7	85.7	39.3
7	Kang et al[32]	With tirofiban	2.9	0	15.9	94.1	63.2
		Without tirofiban	13.9	1.5	19.1	95.8	56.9
8	Pan et al[20]	With tirofiban	12.2	6.1	–	85.4	48.1
		Without tirofiban	31.8	12.4	–	85.3	36.1
9	Zhang et al[19]	With tirofiban	43.5	13.6	22.1	86.4	48.1
		Without tirofiban	51.5	16.7	27.6	83.9	43.3
10	Yi et al[33]	With tirofiban	10.6	4.3	8.5	93.6	51.1
		Without tirofiban	8.9	5.4	7.1	87.3	48.6

Abbreviations: IA, intra-arterial; ICH, intracranial hemorrhage; mRS, modified Rankin Scale; mTICI, modified Thrombolysis in Cerebral Infarction; sICH, symptomatic ICH.

2.7% of the patients in the tirofiban group had sICH, while 8.7% had sICH in the non-tirofiban group. Zhang et al[19] had shown an overall ICH (43% vs. 51%) and sICH (13% vs. 16%) in the tirofiban and non-tirofiban groups, respectively. Zhao et al[23] showed incidence of ICH (36% vs. 33%) and sICH (11% vs. 10%) in the tirofiban versus non-tirofiban groups. In a meta-analysis published by Gong et al[27] in 2020, the IA tirofiban group showed 11.4% sICH, while the control group showed 13% sICH. The possible explanation for the low incidence of ICH in our study in the tirofiban group could be relatively low infarct burden in the tirofiban group compared with the non-tirofiban group (DWI ASPECTS 7.1. vs. 6.7), persistent stenotic lesion in the tirofiban group providing a protective effect on reperfusion hemorrhage, and lower numbers of intravenous thrombolysis in our samples as compared with the literature.

Functional outcome following MT was assessed by mRS. A favorable mRS score of 0 to 2 at 3 months was achieved in 50% of tirofiban group and 67% non-tirofiban group. Functional outcomes were improved by an additional 20% (18 out of 82) using rescue therapy in suboptimally recanalized patients without increasing the risk of hemorrhage. A summary of past literature reviewing the safety and efficacy of IA tirofiban and comparison with our study is shown in ►**Table 5**.

Mortality was seen in 27% of patients in the tirofiban group and 10% in the non-tirofiban group. Six of these 10 deaths in the tirofiban group were in patients with vertebrobasilar occlusion, which are associated with higher mortality irrespective of revascularization. Two deaths were due to other systemic conditions like coronavirus disease pneumonia and aspiration pneumonitis. The remaining two deaths were in patients with anterior circulation stroke. One was due to stent occlusion and ensuing malignant edema; the other had a late reocclusion and holohemispheric infarction. However, with appropriate rescue strategies, 72% of failed or suboptimal recanalization patients achieved optimal target vessel patency, which otherwise would have resulted in higher mortality in these patients.

Limitation of the Study

The study's major limitation is the smaller number of samples in the tirofiban group to comment on safety effectively. Also, we had a lower number of patients who underwent intravenous thrombolysis in the tirofiban group; because of this, subgroup analysis on the safety of tirofiban in the presence of intravenous thrombolysis was not possible. Absence of control group within the suspected ICAD cohort is the other limitation.

Conclusion

Usage of IA tirofiban with or without other adjunct techniques as a rescue therapy during MT in LVO improved recanalization rates without increasing the risk of symptomatic hemorrhage.

Ethical approval

The study was conducted in the Department of Interventional Radiology, Kovai Medical Center and Hospital, Coimbatore, Tamil Nadu, India, after approval by the local ethical and scientific committee.

Conflict of Interest

None declared.

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