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Original research

Bridging thrombolysis in atrial fibrillation stroke is associated with increased hemorrhagic complications without improved outcomes

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ABSTRACT

Background Atrial fibrillation (AF) associated ischemic stroke is associated with worse functional outcomes, less effective recanalization, and increased rates of hemorrhagic complications after intravenous thrombolysis (IVT). Conversely, AF is not associated with hemorrhagic complications or functional outcomes in patients undergoing mechanical thrombectomy (MT). This differential effect of MT and IVT in AF associated stroke raises the question of whether bridging thrombolysis increases hemorrhagic complications in AF patients undergoing MT.

Methods This international cohort study of 22 comprehensive stroke centers analyzed patients with large vessel occlusion (LVO) undergoing MT between June 1, 2015 and December 31, 2020. Patients were divided into four groups based on comorbid AF and IVT exposure. Baseline patient characteristics, complications, and outcomes were reported and compared.

Results 6461 patients underwent MT for LVO. 2311 (35.8%) patients had comorbid AF. In non-AF patients, bridging therapy improved the odds of good 90 day functional outcomes (adjusted OR (aOR) 1.29, 95% CI 1.03 to 1.60, $p=0.025$) and did not increase hemorrhagic complications. In AF patients, bridging therapy led to significant increases in symptomatic intracranial hemorrhage and parenchymal hematoma type 2 (aOR 1.66, 1.07 to 2.57, $p=0.024$) without any benefit in 90 day functional outcomes. Similar findings were noted in a separate propensity score analysis.

Conclusion In this large thrombectomy registry, AF patients exposed to IVT before MT had increased hemorrhagic complications without improved functional outcomes, in contrast with non-AF patients. Prospective trials are warranted to assess whether AF patients represent a subgroup of LVO patients who may benefit from a direct to thrombectomy approach at thrombectomy capable centers.

INTRODUCTION

The role of bridging therapy with intravenous thrombolysis (IVT) in the management of large vessel occlusions (LVOs) undergoing mechanical thrombectomy (MT) remains unclear. Given the high rates of recanalization with MT, it is not known whether the potential for thrombolytic induced recanalization justifies the risk of hemorrhagic complications associated with exposure to IVT. Retrospective studies and a meta-analysis have suggested conflicting results regarding the utility of bridging therapy.^{1–3} Four randomized controlled trials have recently reported similarly mixed results, two demonstrating non-inferiority while the other two were unable to confirm non-inferiority or inferiority.^{4–7} These mixed results are likely due to varying endpoints, but may also reflect a heterogeneous population of stroke patients in which subgroups differentially respond to bridging thrombolysis. While it remains unclear how these recent data will change clinical practice, it is clear that improved patient selection strategies will be required to optimize bridging therapy treatment decisions.

Atrial fibrillation (AF) is a common cause of acute ischemic stroke and is independently associated with more severe stroke syndromes, poor functional outcomes, increased rates of hemorrhagic conversion, and increased mortality after an ischemic stroke, even when controlling for premorbid anti-coagulant use.^{8–12} The lack of ischemic preconditioning likely contributes to the larger territories of hypoperfusion and infarction reported in AF associated strokes.^{8 13 14} There may also be a contribution of larger infarct burden based on larger cardioemboli, although this has been disputed.^{15 16} In patients treated with IVT, comorbid AF diminishes the benefit of thrombolysis and is independently associated with larger infarcts, hemorrhagic complications, and worse clinical outcomes, although this

is not uniformly replicated.^{13 17–19} Interestingly, the experience in MT is different, with no differences in clinical outcomes or hemorrhagic complications in AF associated strokes treated with MT.^{20–22} This may be due to high baseline rates of reperfusion with MT, in combination with procedural advantages in AF associated stroke that lead to faster procedure times and higher rates of first pass success.²⁰

This differential effect of MT and IVT in AF associated stroke raises the question of whether patients with AF associated LVO may be at higher risk for hemorrhagic complications of IVT and benefit from a direct to thrombectomy approach at thrombectomy capable centers. To test this hypothesis, we leveraged a large multicenter, international, real world registry to assess whether hemorrhagic complications and clinical outcomes were modified by exposure to bridging therapy in AF patients undergoing MT.

METHODS

Study population

Patient data were reviewed from the Stroke Thrombectomy and Aneurysm Registry (STAR) that included all patients (18 years of age or older) undergoing MT for acute ischemic stroke at 22 comprehensive stroke centers between June 1, 2015 and December 31, 2020.^{23 24} Patients with both anterior and posterior circulation occlusions were included. Patients were allocated to the AF group if they had an established diagnosis of AF prior to presentation with acute ischemic stroke, or if AF was diagnosed during stroke work-up prior to discharge. The diagnosis of AF was adjudicated at the site level. These data was generated by retrospective review of individual charts at each participating site; diagnostic codes were not used to adjudicated a diagnosis of AF.

To guard against confounding comorbid AF and carotid atherosclerosis, patients were excluded from the analysis if they had both AF and underwent carotid angioplasty or stenting during thrombectomy. The registry did not assess the completeness of the stroke work-up; patients were therefore not excluded due to the presence or absence of any specific diagnostic tests. Additionally, data on antithrombotic usage and comorbid heart failure or valvular disease are not currently reported in the registry. Finally, the intervals between IVT and MT are not available in the registry. This study was approved by the institutional review boards at each participating institution, and informed consent was waived given the retrospective design of the study.

Mechanical thrombectomy

Patient selection for MT was based on operator judgement and discussion with patient families. It was not influenced by this study. Participating centers used different selection criteria for patient eligibility. Investigators had no uniform onset-to-groin cutoff for offering intervention. The frontline thrombectomy approach used was based on operator preference and included aspiration thrombectomy (or ADAPT), stent retriever, primary combined approach or, in a few cases, intracranial angioplasty and stenting. Success of recanalization was reported using the modified Thrombolysis in Cerebral Ischemia (TICI) score performed by the operator at the end of the procedure.²⁵ Postprocedural hemorrhage was assessed using postoperative CT or MRI performed 24 hours after the procedure.

Data collection

Demographic data, admission deficits, severity scores, onset-to-groin time, and IVT use were reviewed from patient charts.

Procedure notes and imaging reports were reviewed for technical variables, reperfusion scores (TICI), and hemorrhage scores. Postprocedural hemorrhage was scored by neuroradiologists based on the European Cooperative Acute Stroke Study (ECASS) II criteria.²⁶ Successful recanalization was defined as a TICI score of 2B or more.

Clinical outcomes

The modified Rankin scale (mRS) was the primary outcome measure. mRS scores were obtained during routinely scheduled follow-up visits with stroke neurologists or advanced practice providers at 90 days post-stroke (± 14 days). In the event patients were discharged to a nursing home or hospice or were unable to attend the clinic visit, telephone encounters were used. Telephone encounters with family were used to confirm the mortality of deceased patients. A good outcome was defined as an mRS score of 0–2 at day 90. Postprocedural National Institutes of Health Stroke Scale (NIHSS) scores (within 24 hours), NIHSS score at discharge and/or follow-up were also available for a subset of patients.

Complications

Procedural notes were reviewed for intraoperative complications, including the type of complication and need for intervention. Additionally, postprocedural hemorrhage was evaluated by neuroradiology on postoperative CT or MRI imaging (24 hours) based on ECASS-II criteria, including parenchymal hematoma type 2 (PH2).²⁶ Symptomatic intracranial hemorrhage (sICH) was defined as postprocedural hemorrhage associated with an increase of at least 4 on the NIHSS.

Statistical analysis

Statistical analyses were performed in SPSS V.25 (IBM) and GraphPad Prism 9 (GraphPad, California, USA). Univariate testing was performed using the Student's t-test, Mann-Whitney test, or χ^2 test for parametric, non-parametric, and categorical variables, respectively. Multivariate analysis was then performed using independent models for different outcome measures. Variables included in regression analysis were predetermined variables (age, sex, admission NIHSS, comorbidities), and variables with $p < 0.1$ on univariate testing. To avoid bias in excluding patients with incomplete data, we used multiple imputations to handle missing baseline variables (race, onset-to-groin, sex, and other comorbidities), and Rubin's rule was then used to approximate coefficients. Missing data were less than 10% of observations for each variable. A total of 10 imputations was performed for each model. Clinical severity, presence of atrial fibrillation, procedural variables, and outcome variables were not imputed. Logistic regression models were used for categorical variables (eg, good outcome). In the subset of patients with comorbid AF, propensity score matched subgroups based on the use of IVT were identified using the nearest neighbor algorithm while balancing demographic, baseline, and admission variables. A p value < 0.05 was considered statistically significant.

RESULTS

A total of 6461 patients underwent MT for LVO at 22 stroke centers during the study period. We divided patients into four groups based on comorbid AF and exposure to IVT prior to MT. Of all patients included in the study, 3050 (47.2%) were treated with IVT prior to MT (table 1). Comorbid AF was noted in 2311 (35.8%) patients, of whom 1036 (44.8%) were also treated with

Table 1 Patient demographic, admission, technical, radiographic, and clinical outcome variables

Variable	AF				P value	No AF				
	IVT		No IVT			IVT		No IVT		
	N		N			N		N		
Demographics										
Age (mean (SD))	1036	76 (11)	1275	76 (11)	0.935	2104	65 (15)	2046	65 (15)	0.648
Female (n (%))	1036	559 (54)	1275	688 (54)	0.999	2104	1010 (48)	2046	986 (48)	0.928
White race (n (%))	524	385 (74)	599	417 (70)	0.154	1140	753 (66)	1000	653 (65)	0.749
Comorbidities (n (%))										
Diabetes	1029	293 (29)	1273	389 (31)	0.276	2105	491 (23)	2045	596 (29)	0.001
Hypertension	1036	840 (81)	1275	1070 (84)	0.082	2104	1407 (67)	2046	1477 (72)	0.001
Hyperlipidemia	1034	442 (43)	1273	633 (50)	0.001	2104	813 (39)	2045	849 (41)	0.065
Previous stroke	818	123 (15)	1083	246 (23)	0.001	1650	197 (12)	1796	325 (18)	0.001
Pre-stroke mRS (0–2)	714	644 (90)	909	792 (87)	0.065	1552	1457 (94)	1522	1381 (91)	0.001
Admission variables										
Admission NIHSS (mean (SD))	1032	16 (6)	1263	16 (7)	0.226	2086	15 (7)	2019	15 (8)	0.052
ASPECT score >6 (n (%))	480	418 (87)	525	451 (86)	0.065	1806	1575 (87)	802	700 (87)	0.944
Onset-to-groin time (hours) (mean (SD))	889	4.3 (3)	1061	7.7 (7)	0.001	1871	4.3 (3)	1696	10 (14)	0.001
Procedural variables										
Procedure time (min) (mean (SD))	942	51 (41)	1138	48 (39)	0.173	1889	55 (58)	1856	52 (47)	0.73
Total attempts (mean (SD))	865	2.1 (1.5)	1158	2.2 (1.6)	0.05	1688	2.1 (1.5)	1767	2.4 (1.8)	0.001
Final TIC1 score (n (%))	985		1235		0.594	1956		1960		0.572
0–2A		152 (15)		202 (16)			309 (16)		323 (16)	
2B–3		833 (85)		1033 (84)			1647 (84)		1637 (84)	
Complications (n (%))	755	47 (6)	1195	63 (6)	0.936	1656	114 (7)	1697	125 (7.4)	0.592
Hemorrhage (PH2/sICH) (n (%))	994	91 (9.2)	1186	82 (6.9)	0.0477	1995	140 (7)	1900	129 (6.8)	0.801
Outcome (n (%))										
mRS: 90 days	879		986		0.083	1782		1709		0.001
mRS 0–2		295 (34)		294 (30)			822 (46)		605 (35)	
mRS 3–6		584 (66)		692 (70)			960 (54)		1104 (65)	
Mortality: 90 days	879	222 (25)	986	300 (30)	0.013	1782	324 (18)	1709	415 (24)	0.001

Statistical tests were done using t tests, χ^2 tests, or Mann-Whitney tests.

AF, atrial fibrillation; ASPECT, Alberta stroke program early CT score; ICA, internal carotid artery; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PH2, parenchymal hematoma type 2; sICH, symptomatic intracranial hemorrhage; TIC1, Thrombolysis in Cerebral Infarction.

IVT prior to MT. In 4150 non-AF patients, 2104 (50.7%) were exposed to IVT prior to MT.

Baseline patient and presentation characteristics are reported in table 1 and online supplemental table 1. AF patients were more likely to be older, female, white, and have vascular risk factors, including hypertension and hyperlipidemia ($p < 0.05$, online supplemental table 1). Presentation characteristics also differed, with higher NIHSS scores on admission, lower Alberta stroke program early CT score (ASPECTS), and lower rates of IVT prior to MT (online supplemental table 1).

When comparing AF patients with and without IVT exposure, patients receiving IVT had lower rates of hyperlipidemia and previous ischemic stroke (table 1). Patients receiving IVT had significantly shorter onset-to-groin times (4.3 vs 7.7 hours, respectively, $p < 0.001$), slightly fewer total endovascular passes at the clot (2.1 vs 2.2, respectively, $p < 0.05$), and lower mortality at 90 days (25% vs 30%, respectively, $p < 0.013$) in univariable analysis. Similar results were noted in non-AF patients undergoing IVT (table 1).

We assessed whether bridging thrombolysis was associated with hemorrhagic complications after MT. In univariable analysis, there was no significant difference in the rates of sICH or PH2 (sICH/PH2) hemorrhage between non-AF patients with or

without bridging therapy (7.0% vs 6.8%, $p > 0.05$), but there were increased rates of hemorrhagic complications in AF patients exposed to IVT (9.2% vs 6.9%, $p < 0.05$, figure 1A). Under multivariable binary logistic regression assumptions, patients with comorbid AF who received IVT were independently associated with higher rates of sICH/PH2 (adjusted OR (aOR) 1.41, 95% CI 1.0.1 to 1.97, $p = 0.042$ (online supplemental table 2). Procedural complications and increased number of thrombectomy attempts were also associated with increased hemorrhagic complications. When restricting the analysis to only patients with AF, IVT was independently associated with sICH/PH2 (aOR 1.66, 1.07 to 2.57, $p = 0.024$, (online supplemental table 2).

Good functional outcomes were assessed by ordinal shift analysis. Exposure to IVT was associated with improved functional outcomes in non-AF patients, but there was no improvement in AF patients (figure 1B). In multivariable binary logistic regression analysis, exposure to IVT improved the odds of good functional outcomes in the full cohort (aOR 1.28, 1.07 to 1.54, $p = 0.006$) and non-AF patients (aOR 1.29, 1.03–1.60, $p = 0.025$) but not in AF patients (aOR 1.28, 0.94 to 1.74, $p = 0.11$, table 2, figure 1C).

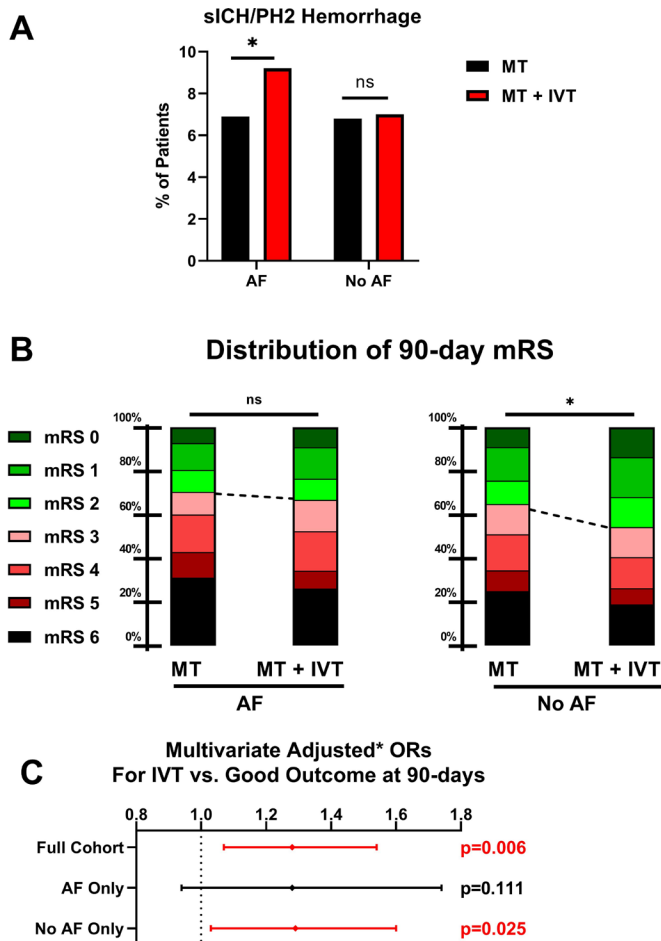


Figure 1 Impact of bridging thrombolysis on symptomatic hemorrhage and functional outcomes in atrial fibrillation (AF) associated stroke undergoing mechanical thrombectomy. (A) Rates of symptomatic intracranial hemorrhage (sICH) or parenchymal hematoma type 2 (PH2) hemorrhage in patients with or without bridging therapy divided by AF status. Proportion statistics performed using a z score test. IVT, intravenous thrombolysis; MT, mechanical thrombectomy. (B) Distribution of 90 day modified Rankin Scale (mRS) scores by AF status and use of bridging therapy. Comparison of shift performed using the χ^2 test. (C) Results of multivariable logistic regression for odds of good outcome (mRS 0–2) with intravenous tissue plasminogen activator (IV-tPA) use in patients with AF, no AF, or full cohort. Variables were adjusted for: female gender; age; diabetes mellitus; hypertension; hyperlipidemia; baseline mRS; admission National Institutes of Health Stroke Scale score; anterior location; Alberta stroke program early CT score; onset-to-groin (hours); procedure time (min); successful recanalization; and complications. * $p < 0.05$.

We further evaluated the outcome observations in AF patients using propensity score matching analysis. A subset of 1404 AF patients who underwent MT were matched on the baseline variables outlined in table 3 and bifurcated by bridging therapy with IVT. Bridging therapy did not improve functional outcomes or mortality in AF patients, but did lead to a significant increase in sICH/PH2 (OR 1.56, 1.05 to 2.29, $p = 0.032$).

DISCUSSION

Given the historically low recanalization efficacy and increased hemorrhagic complications of IVT for LVOs in AF associated stroke specifically, it is unclear whether bridging therapy with IVT is beneficial in AF patients undergoing MT.^{27–29} We used a

large, real world cohort study from an international thrombectomy registry of 6461 patients to test whether bridging therapy was associated with increased hemorrhagic complications or improved clinical outcomes in AF-associated LVO undergoing MT.

In univariable analysis, AF patients exposed to bridging therapy had significantly higher rates of sICH. When comparing the four cohorts of patients divided by comorbid AF and exposure to bridging therapy, comorbid AF with bridging therapy was independently associated with sICH compared with all other patients. Similarly, when evaluating only AF patients, bridging therapy was independently associated with sICH. Importantly, bridging therapy improved functional outcomes in non-AF patients, as assessed by mRS shift analysis, but that benefit was not observed in AF patients. Similar increases in sICH without improvement in functional outcomes were observed in a propensity score matched analysis in AF patients, with and without IVT. Together, these data confirm previously reported observations that IVT complications are increased in AF patients, and newly demonstrate that in AF patients undergoing MT, bridging therapy increased sICH without improving functional outcomes.^{13 17 18} These observations likely reflect the lack of ischemic pre-conditioning with sudden cardioembolism, resulting in narrower therapeutic windows and larger territories at risk for infarction and hemorrhagic conversion after IVT.^{8 13 14}

These data suggest that a direct to thrombectomy approach in thrombectomy capable centers may be a safer reperfusion strategy that capitalizes on the procedural advantages of AF in MT and avoids the increased hemorrhagic complications of IVT in this population.²⁰ Consistent with these observations, a recently announced but not yet reported meta-analysis of two randomized clinical trials on bridging therapy observed a similar observation in their subgroup analysis of 193 non-AF and 245 AF patients. Investigators reported a non-significant trend towards increased sICH and significant increases in both any complicating hemorrhage and 90 day mortality in AF patients exposed to bridging therapy prior to MT.³⁰

Our results contribute to the ongoing efforts to optimize patient selection for bridging therapy. Within the limitations of retrospective, non-randomized data, our observations reflect the heterogeneous results recently reported in four randomized controlled trials, suggesting that a differential effect of bridging therapy in specific patient subgroups may explain the mixed results.^{4–7} In this context, bridging therapy is likely to remain the standard of care at most centers unless subgroup specific harm can be demonstrated. Our data, in combination with the recent reports from DEVT and SKIP, highlight AF patients as a particularly high risk subgroup that may benefit from a direct to thrombectomy reperfusion strategy.³⁰ IVT currently remains the standard of care for eligible patients, but randomized trials will be essential to determine whether AF patients with an acute LVO represent a subgroup of patients who would benefit from a direct to thrombectomy approach at thrombectomy capable centers.

Our study nevertheless has several limitations. There was significant confounding by indication for pre-morbid anticoagulant use in the AF cohort, and this was further amplified by the lack of any pre-morbid antithrombotic data in the registry. Nevertheless, the absolute contraindication to IVT in the setting of anticoagulation makes it unlikely that a significant percentage of AF patients bridged with IVT were on therapeutic anticoagulation, although this has been reported in rare cases.^{31 32} Conversely, therapeutic anticoagulation was likely enriched in the AF cohort that did not receive IVT. In fact, at least two

Table 2 Multivariable binary logistic regression for predictors of good outcome (modified Rankin Scale score 0–2) at 90 days

Variable	Full cohort n=3070			AF cohort n=1045			No AF cohort n=2025		
	aOR	95% CI	P value	aOR	95% CI	P value	aOR	95% CI	P value
Female gender	0.98	0.82 to 1.15	0.768	0.94	0.7 to 1.27	0.692	1	0.82 to 1.23	0.969
Age	0.97	0.97 to 0.98	0.001	0.96	0.95 to 0.98	0.001	0.97	0.96 to 0.98	0.001
Diabetes mellitus	0.65	0.54 to 0.79	0.001	0.55	0.39 to 0.77	0.001	0.7	0.56 to 0.89	0.003
Hypertension	0.85	0.69 to 1.04	0.11	0.85	0.57 to 1.27	0.436	0.83	0.65 to 1.05	0.119
Hyperlipidemia	1.06	0.89 to 1.26	0.504	0.98	0.73 to 1.32	0.888	1.1	0.88 to 1.36	0.406
Prestroke mRS 0–2	5.24	3.32 to 8.26	0.001	3.53	1.85 to 6.74	0.001	7.13	3.73 to 13.65	0.001
Admission NIHSS score	0.91	0.89 to 0.92	0.001	0.9	0.88 to 0.92	0.001	0.91	0.89 to 0.92	0.001
Anterior location	1.03	0.79 to 1.36	0.812	0.86	0.50 to 1.48	0.582	1.1	0.80 to 1.51	0.554
ASPECT score >6	0.99	0.63 to 1.57	0.973	0.96	0.38 to 2.40	0.919	1.03	0.63 to 1.66	0.916
IV-tPA use	1.28	1.07 to 1.54	0.006	1.28	0.94 to 1.74	0.111	1.29	1.03 to 1.60	0.025
Onset-to-groin (hours)	0.97	0.95 to 0.98	0.001	0.97	0.94 to 1.00	0.033	0.97	0.95 to 0.99	0.001
Procedure time (min)	0.58	0.49 to 0.68	0.001	0.64	0.48 to 0.85	0.002	0.56	0.46 to 0.68	0.001
Successful recanalization	3.33	2.43 to 4.56	0.001	2.97	1.69 to 5.22	0.001	3.5	2.39 to 5.10	0.001
Complications	0.59	0.42 to 0.85	0.004	0.62	0.33 to 1.19	0.149	0.58	0.38 to 0.89	0.013

AF, atrial fibrillation; aOR, adjusted OR; ASPECT, Alberta stroke program early CT score; IV-tPA, intravenous tissue plasminogen activator; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

registries have reported anticoagulation rates of more than 20% in unselected patients undergoing MT.^{33 34} While the absence of antithrombotic data is an important limitation, the likely enrichment of anticoagulant use in the non-bridging therapy patients (who suffered less hemorrhagic complications) highlights a striking difference between these cohorts. On the other hand, antiplatelet use is unlikely to correlate with IVT candidacy, and thus the lack of antiplatelet data remains a limitation. Second, the adjudicated stroke mechanism was not reported for each patient. Instead, we used comorbid AF as a surrogate for the mechanism,

likely underestimating the rate of non-cardioembolic stroke in patients with comorbid AF. Although lacunar and atheroembolic strokes occur in the setting of AF, we selected for LVOs and excluded patients with carotid interventions to minimize these confounds, respectively.^{35 36} Third, angiographic, hemorrhagic, and clinical outcomes were locally reported without central adjudication. Fourth, as a retrospective registry, we cannot exclude selection bias, particularly with decisions for continued recanalization attempts to improve the angiographic outcome. Fifth, due to variably completed datasets in the registry, the analysis was limited by the use of multiple imputations to handle missing baseline variables in a subset of patients. However, the use of multiple imputation also limited bias by limiting the exclusion of patients with missing data. Finally, our analysis was not powered to dissect whether the observed associations were restricted to anterior and/or posterior circulation strokes.

Given the historically low recanalization efficacy and increased hemorrhagic complications of IVT for LVOs in AF associated stroke, the role of bridging thrombolysis in AF patients undergoing MT is unclear.^{27–29 37} In this large registry of 6461 MT patients, bridging therapy with IVT in AF patients was independently associated with increased rates of sICH and no improvement in functional outcomes, in contrast with non-AF patients. Prospective trials are warranted to assess whether AF patients with an acute LVO represent a subgroup of patients who may benefit from a direct to thrombectomy approach at thrombectomy-capable centers.

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Table 3 Baseline and outcome variables in propensity score matched subset of atrial fibrillation patients dichotomized by intravenous thrombolysis use

Variable	No IVT (n=702)	IVT (n=702)	P value
Baseline			
Age (mean (SD))	76 (10)	76 (11)	0.380
Female gender (n (%))	378 (54)	371 (53)	0.748
Diabetes mellitus (n (%))	213 (30)	203 (29)	0.599
Hypertension (n (%))	580 (82)	566 (81)	0.37
Hyperlipidemia (n (%))	322 (46)	297 (43)	0.197
Prestroke mRS 0–2 (n (%))	641 (91)	651 (93)	0.786
Admission NIHSS (mean (SD))	16 (6.8)	16 (6.5)	0.637
Posterior location (n (%))	54 (7.7)	44 (6.3)	0.346
ASPECTS >6 (n (%))	670 (95)	670 (95)	1.00
Outcome			
Successful recanalization (n (%))	601 (86)	594 (85)	0.653
90 day mRS (0–2) (n (%))	217 (30.9)	231 (32.9)	0.342
Mortality (%)	27.30	25.70	0.593
sICH/PH2 (n (%))	46 (6.6)	69 (9.8)	0.032

ASPECT, Alberta stroke program early CT score; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; PH2, parenchymal hematoma type 2; sICH, symptomatic intracranial hemorrhage.

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Supplemental Table 1. Demographic, Admission, Technical, Radiographic and Clinical Outcome Variables in Patients with and without Atrial Fibrillation.

Variable	AF		No AF		P-value
	N	Mean (SD) Median [IQR] N (%)	N	Mean (SD) Median [IQR] N (%)	
Demographics					
Age	2311	76 (11)	4150	65 (15)	0.001
Female	2311	1996 (48)	4150	1247 (54)	0.001
White Race	1123	1406 (66)	2140	802 (71)	0.001
Comorbidities					
Diabetes	2302	1087 (26)	4150	682 (30)	0.003
Hypertension	2311	2884 (69)	4150	1910 (83)	0.001
Hyperlipidemia	2307	1662 (40)	4149	1075 (47)	0.001
Prior Stroke	1901	522 (15)	3446	369 (19)	0.001
Pre-stroke mRS (0-2)	1623	2838 (92)	3074	1436 (88)	0.001
Admission Variables					
Admission NIHSS	2295	15 (7)	4216	16 (7)	0.001
ASPECT Score > 6	1005	2275 (87)	2608	869 (86)	> 0.2
Onset-to-groin time (hr)	1950	7 (10.3)	3567	6.1 (5.8)	0.001
Procedural Variables					
Procedure time (min)	2080	53.5 (52.9)	3745	49.4 (39.9)	0.002
Total Attempts	2023	2.3 (1.7)	3455	2.2 (1.6)	0.035
Final TICI score	2220		3916		> 0.2
0-2A		632 (16)	3916	354 (16)	
2B-3		3284 (84)	3916	1866 (84)	
Complications	1950	239 (7)	3353	110 (6)	0.035
Hemorrhage (PH2/sICH)	2180	269 (7)	3895	173 (8)	0.138
Outcome					
mRS: Discharge	1865	4 [4]	3491	4 [4]	0.001
mRS: 90-days	1865		3491		> 0.2
mRS 0-2		1427 (41)	3491	589 (32)	
mRS 3-6		2064 (59)	3491	1276 (68)	
Mortality: 90 days	1865	739 (21)	3491	522 (28)	0.001

AF, atrial fibrillation; ASPECT, Alberta stroke program early CT score; mRS, modified Rankin Scale; NIHSS, National Institute of Health Stroke Scale; PH2, parenchymal hematoma type II (ECASS-II criteria); sICH, symptomatic intracranial hemorrhage; TICI, thrombolysis in cerebral infarction score. Statistical tests were done using t-tests, chi squared tests (Chi-sq), or Mann-Whitney tests (MW).

Supplemental Table 2. Multivariable Binary Logistic Regression for Predictors of Post-procedural sICH/PH2 hemorrhage.

Supplemental Table 2. Multivariate Logistic Regression for Predictors of Post-procedural sICH/PH2 hemorrhage.			
Variable	Coefficient	95% CI	p-value
Full Cohort			
Model : Logistic Regression, N = 3128			
Age	1.01	1 - 1.02	0.07
White Race	0.84	0.62 - 1.13	0.239
Diabetes Mellitus	1.24	0.94 - 1.64	0.129
Hypertension	0.99	0.71 - 1.37	0.938
Hyperlipidemia	0.91	0.7 - 1.18	0.476
Baseline mRS 0-2	1.44	0.88 - 2.36	0.151
Admission NIHSS	1.01	0.99 - 1.03	0.385
Location: Posterior	1.75	1.08 - 2.85	0.024
ASPECTS > 6	1.02	0.53 - 1.99	0.947
AFIB+IV-tPA Use	1.41	1.01 - 1.97	0.042
Onset-to-Groin	1	0.99 - 1.02	0.888
Number of Passes	1.12	1.05 - 1.2	0.001
Successful Recanalization	0.84	0.6 - 1.18	0.322
Complications	2.99	2.07 - 4.33	0.001
IA-tPA Use	1.14	0.79 - 1.65	0.483
AF Cohort Only			
Model : Logistic Regression, N = 1229			
Age	0.997	0.98 - 1.02	0.762
White Race	0.59	0.35 - 0.97	0.039
Diabetes Mellitus	1.28	0.81 - 2.03	0.287
Hypertension	1.28	0.68 - 2.44	0.445
Hyperlipidemia	0.85	0.55 - 1.31	0.457
Baseline mRS 0-2	1.53	0.71 - 3.33	0.279
Admission NIHSS	1.01	0.98 - 1.04	0.528
Location: Posterior	2.38	0.84 - 6.72	0.103
ASPECTS > 6	1.63	0.36 - 7.4	0.517
IV-tPA Use	1.66	1.07 - 2.57	0.024
Onset-to-Groin	1.02	0.99 - 1.05	0.208
Number of Passes	1.11	0.99 - 1.25	0.062
Successful Recanalization	0.6	0.35 - 1.04	0.067
Complications	3.14	1.68 - 5.87	0.0001
IA-tPA Use	1.15	0.63 - 2.13	0.646

ASPECT, Alberta stroke program early CT score; IA-tPA, intra-arterial thrombolysis; IV-tPA, intravenous thrombolysis; PH2, parenchymal hematoma type II (ECASS-II criteria); sICH, symptomatic intracranial hemorrhage; TICI, thrombolysis in cerebral infarction score.



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Dr. Akbik has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Ali	2. Surname (Last Name) Alawieh	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
6. Manuscript Identifying Number (if you know it) n/a		

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Are there any relevant conflicts of interest? Yes No

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Are there any relevant conflicts of interest? Yes No

Section 4. Intellectual Property – Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No



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Dr. Alawieh has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Adam	2. Surname (Last Name) Arthur	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
6. Manuscript Identifying Number (if you know it) n/a		

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Are there any relevant conflicts of interest? Yes No

If yes, please fill out the appropriate information below.

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Balt	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Johnson and Johnson	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Medtronic	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Microvention	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Penumbra	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Scientia	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Siemens	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Stryker	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Arthur

2



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Section 4. Intellectual Property -- Patents & Copyrights

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Dr. Arthur reports grants and personal fees from Balt, personal fees from Johnson and Johnson, grants and personal fees from Medtronic, grants and personal fees from Microvention, grants and personal fees from Penumbra, personal fees from Scientia, grants and personal fees from Siemens, grants and personal fees from Stryker, outside the submitted work; .

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Section 1. Identifying Information

1. Given Name (First Name) C. Michael 2. Surname (Last Name) Cawley 3. Date 12-May-2021

4. Are you the corresponding author? Yes No Corresponding Author's Name
Drs. Jonathan Grossberg and Dr. Alex Spiotta

5. Manuscript Title
Bridging Thrombolysis in Atrial Fibrillation Associated Stroke

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Roberto	2. Surname (Last Name) Crosa	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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Dr. Crosa has nothing to disclose.

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1. Given Name (First Name) Travis	2. Surname (Last Name) Dumont	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Kyle	2. Surname (Last Name) Fargen	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
6. Manuscript Identifying Number (if you know it) n/a		

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Are there any relevant conflicts of interest? Yes No

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Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No



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Dr. Fargen has nothing to disclose.

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Section 1. Identifying Information

1. Given Name (First Name) Wuwei	2. Surname (Last Name) Feng	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
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ICMJE Form for Disclosure of Potential Conflicts of Interest

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1. Given Name (First Name) W. Christopher	2. Surname (Last Name) Fox	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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1. Given Name (First Name) Benjamin	2. Surname (Last Name) GORY	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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Are there any relevant conflicts of interest? Yes No

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Are there any relevant conflicts of interest? Yes No

If yes, please fill out the appropriate information below.

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Georgia Research Alliance	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Emory Medical Center Foundation	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Cognition	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Stock Options
Department of Defense SC2i	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
NTI	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Own Equity



ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 4. Intellectual Property – Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No

Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

- Yes, the following relationships/conditions/circumstances are present (explain below):
 No other relationships/conditions/circumstances that present a potential conflict of interest

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Section 6. Disclosure Statement

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Dr. Grossberg reports grants from Georgia Research Alliance, grants from Emory Medical Center Foundation, non-financial support from Cognition, grants from Department of Defense SC2i, other from NTI, outside the submitted work; .

Evaluation and Feedback

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Brian	2. Surname (Last Name) Howard	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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Are there any relevant conflicts of interest? Yes No

Section 4. Intellectual Property – Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No



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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Pascal	2. Surname (Last Name) Jabbour	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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Section 4. Intellectual Property – Patents & Copyrights

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Peter	2. Surname (Last Name) Kan	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
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Section 1. Identifying Information

1. Given Name (First Name) Salah	2. Surname (Last Name) Keyrouz	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
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1. Given Name (First Name) Ilko	2. Surname (Last Name) Maier	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
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4. Intellectual Property.

This section asks about patents and copyrights, whether pending, issued, licensed and/or receiving royalties.

5. Relationships not covered above.

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Definitions.

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Non-Financial Support: Examples include drugs/equipment supplied by the entity, travel paid by the entity, writing assistance, administrative support, etc.

Other: Anything not covered under the previous three boxes

Pending: The patent has been filed but not issued

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Licensed: The patent has been licensed to an entity, whether earning royalties or not

Royalties: Funds are coming in to you or your institution due to your patent



ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) J	2. Surname (Last Name) Mocco	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
6. Manuscript Identifying Number (if you know it) n/a		

Section 2. The Work Under Consideration for Publication

Did you or your institution **at any time** receive payment or services from a third party (government, commercial, private foundation, etc.) for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.)?

Are there any relevant conflicts of interest? Yes No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a row. Excess rows can be removed by pressing the "X" button.

Name of Institution/Company	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Microvention	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Research Support
Penumbra	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Research Support
Stryker	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Research Support

Section 3. Relevant financial activities outside the submitted work.

Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the "Add +" box. You should report relationships that were **present during the 36 months prior to publication**.

Are there any relevant conflicts of interest? Yes No

If yes, please fill out the appropriate information below.

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Cerebrotech	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor and consultant



ICMJE Form for Disclosure of Potential Conflicts of Interest

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Imperative Care	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor and Consultant
Endostream	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor and Consultant
Viseon	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor and Consultant
BlinkTBI	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor
Serenity	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor
Cardinal Consulting	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor
NTI	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor
RIST	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor and Consultant
Viz.ai	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor and Consultant
Synchron	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Investor

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No

Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

- Yes, the following relationships/conditions/circumstances are present (explain below):
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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Dr. Mocco reports other from Microvention, other from Penumbra, other from Stryker, during the conduct of the study; other from Cerebrotech, other from Imperative Care, other from Endostream, other from Viseon, other from BlinkTBI, other from Serenity, other from Cardinal Consulting, other from NTI, other from RIST, other from Viz.ai, other from Synchron, outside the submitted work; .

Evaluation and Feedback

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Fadi	2. Surname (Last Name) Nahab	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
6. Manuscript Identifying Number (if you know it) n/a		

Section 2. The Work Under Consideration for Publication

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Are there any relevant conflicts of interest? Yes No

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Are there any relevant conflicts of interest? Yes No

Section 4. Intellectual Property – Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No



ICMJE Form for Disclosure of Potential Conflicts of Interest

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Section 6. Disclosure Statement

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Dr. Nahab has nothing to disclose.

Evaluation and Feedback

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Marios-Nikos	2. Surname (Last Name) Psychogios	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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Are there any relevant conflicts of interest? Yes No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? Yes No

Section 4. Intellectual Property – Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No



ICMJE Form for Disclosure of Potential Conflicts of Interest

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Dr. Psychogios has nothing to disclose.

Evaluation and Feedback

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Reade	2. Surname (Last Name) De Leacy	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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Are there any relevant conflicts of interest? Yes No

If yes, please fill out the appropriate information below.

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Cerenovus	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Scientific Advisory Board
Penumbra	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Consultant
Siemens Healthineers	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Consultant
Imperative Care	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Consultant



ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 4. Intellectual Property – Patents & Copyrights

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Dr. De Leacy reports personal fees from Cerenovus, personal fees from Penumbra, personal fees from Siemens Healthineers, personal fees from Imperative Care, outside the submitted work; .

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Alejandro	2. Surname (Last Name) Spiotta	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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Are there any relevant conflicts of interest? Yes No

If yes, please fill out the appropriate information below. If you have more than one entity press the "ADD" button to add a row. Excess rows can be removed by pressing the "X" button.

Name of Institution/Company	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
STAR Research Grant	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Penumbra, Medtronic, Stryker

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Are there any relevant conflicts of interest? Yes No

If yes, please fill out the appropriate information below.

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Medtronic	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Penumbra	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Stryker	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	



ICMJE Form for Disclosure of Potential Conflicts of Interest

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
Cerenovus	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
RAPID AI	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Terumo	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Siemens	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Section 4. Intellectual Property -- Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No

Section 5. Relationships not covered above

Are there other relationships or activities that readers could perceive to have influenced, or that give the appearance of potentially influencing, what you wrote in the submitted work?

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Section 6. Disclosure Statement

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Dr. Spiotta reports grants from STAR Research Grant, during the conduct of the study; grants and personal fees from Medtronic, grants and personal fees from Penumbra, grants and personal fees from Stryker, personal fees from Cerenovus, grants from RAPID AI, personal fees from Terumo, personal fees from Siemens, outside the submitted work; .



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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Robert	2. Surname (Last Name) Starke	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
6. Manuscript Identifying Number (if you know it) n/a		

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Are there any relevant conflicts of interest? Yes No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? Yes No

Section 4. Intellectual Property – Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No



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Dr. Starke has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Stacey	2. Surname (Last Name) Wolfe	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
6. Manuscript Identifying Number (if you know it) n/a		

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Are there any relevant conflicts of interest? Yes No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? Yes No

Section 4. Intellectual Property – Patents & Copyrights

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Section 6. Disclosure Statement

Based on the above disclosures, this form will automatically generate a disclosure statement, which will appear in the box below.

Dr. Wolfe has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) ANSAAR	2. Surname (Last Name) RAI	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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Are there any relevant conflicts of interest? Yes No

Section 3. Relevant financial activities outside the submitted work.

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Are there any relevant conflicts of interest? Yes No

If yes, please fill out the appropriate information below.

Name of Entity	Grant?	Personal Fees?	Non-Financial Support?	Other?	Comments
STRYKER NEUROVASCULAR	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
CERENOVUS	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Section 4. Intellectual Property – Patents & Copyrights

Do you have any patents, whether planned, pending or issued, broadly relevant to the work? Yes No



ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 5. Relationships not covered above

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Dr. RAI reports personal fees from STRYKER NEUROVASCULAR, personal fees from CERENOVUS, outside the submitted work; .

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Owen	2. Surname (Last Name) Samuels	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
5. Manuscript Title Bridging Thrombolysis in Atrial Fibrillation Associated Stroke		
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Are there any relevant conflicts of interest? Yes No

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Dr. Samuels has nothing to disclose.

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ICMJE Form for Disclosure of Potential Conflicts of Interest

Section 1. Identifying Information

1. Given Name (First Name) Frank	2. Surname (Last Name) Tong	3. Date 12-May-2021
4. Are you the corresponding author?	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No	Corresponding Author's Name Drs. Jonathan Grossberg and Dr. Alex Spiotta
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Are there any relevant conflicts of interest? Yes No

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Dr. Tong has nothing to disclose.

Evaluation and Feedback

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ICMJE DISCLOSURE FORM

Date: 9/20/2021

Your Name: Jan Liman

Manuscript Title: Bridging Thrombolysis in Atrial Fibrillation Stroke is Associated With Increased Hemorrhagic Complications Without Improved Outcomes

Manuscript Number (if known): neurintsurg-2021-017954.R1

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