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Safety Outcomes of Mechanical Thrombectomy Versus Combined Thrombectomy and Intravenous Thrombolysis in Tandem Lesions

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Abstract

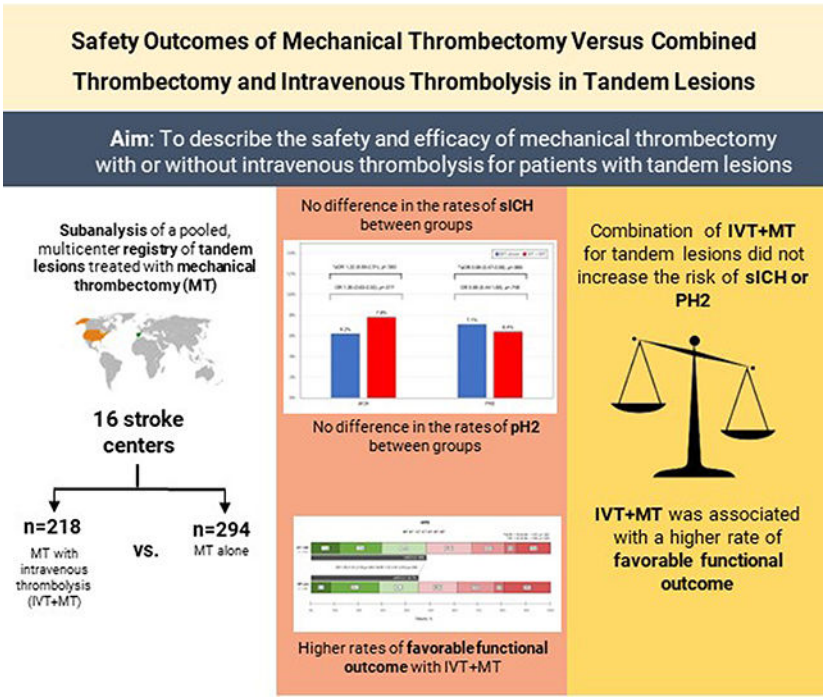
BACKGROUND: We aimed to describe the safety and efficacy of mechanical thrombectomy (MT) with or without intravenous thrombolysis (IVT) for patients with tandem lesions and whether using intraprocedural antiplatelet therapy influences MT's safety with IVT treatment.

METHODS: This is a subanalysis of a pooled, multicenter cohort of patients with acute anterior circulation tandem lesions treated with MT from 16 stroke centers between January 2015 and December 2020. Primary outcomes included symptomatic intracranial hemorrhage (sICH) and parenchymal hematoma type 2. Additional outcomes included hemorrhagic transformation, successful reperfusion (modified Thrombolysis in Cerebral Infarction score 2b-3), complete reperfusion (modified Thrombolysis in Cerebral Infarction score 3), favorable functional outcome (90-day modified Rankin Scale score 0–2), excellent functional outcome (90-day modified Rankin Scale score 0–1), in-hospital mortality, and 90-day mortality.

RESULTS: Of 691 patients, 512 were included (218 underwent IVT+MT and 294 MT alone). There was no difference in the risk of sICH (adjusted odds ratio [aOR], 1.22 [95% CI, 0.60–2.51]; *P*=0.583), parenchymal hematoma type 2 (aOR, 0.99 [95% CI, 0.47–2.08]; *P*=0.985), and hemorrhagic transformation (aOR, 0.95 [95% CI, 0.62–1.46]; *P*=0.817) between the IVT+MT and MT alone groups after adjusting for confounders. Administration of IVT was associated with an increased risk of sICH in patients who received intravenous antiplatelet therapy (aOR, 3.04 [95% CI, 0.99–9.37]; *P*=0.05). The IVT+MT group had higher odds of a 90-day modified Rankin Scale score 0 to 2 (aOR, 1.72 [95% CI, 1.01–2.91]; *P*=0.04). The odds of successful reperfusion, complete reperfusion, 90-day modified Rankin Scale score 0 to 1, in-hospital mortality, or 90-day mortality did not differ between the IVT+MT versus MT alone groups.

CONCLUSIONS: Our study showed that the combination of IVT with MT for tandem lesions did not increase the overall risk of sICH, parenchymal hematoma type 2, or overall hemorrhagic transformation independently of the cervical revascularization technique used. However, intraprocedural intravenous antiplatelet therapy during acute stent implantation might be associated with an increased risk of sICH in patients who received IVT before MT. Importantly, IVT+MT treatment was associated with a higher rate of favorable functional outcomes at 90 days.

Graphical Abstract



Keywords

intracranial hemorrhage; reperfusion; stroke; thrombectomy

Tandem lesions (TLs) account for about 10% to 20% of large vessel occlusion (LVO) strokes.[1–5] Mechanical thrombectomy (MT) has demonstrated a safe and effective profile for treating TLs.[6–9] However, the optimal acute cervical endovascular approaches to optimize outcomes, including angioplasty alone versus angioplasty and stenting, are currently under investigation.[6,10,11] Furthermore, the role of intravenous thrombolysis (IVT) in combination with different treatment options is incompletely defined.

In an international survey performed by our group for treating TLs, the use of IVT+MT was controversial.[12] Antiplatelet therapy (APT) during endovascular treatment for TLs may be safe and associated with lower mortality.[13] However, when coadministered with IVT in patients undergoing acute carotid stenting, there was significant concern regarding the increased risk of hemorrhagic complications.[14] Furthermore, TLs are considered a predictor of poor reperfusion after IVT alone due to underlying atherosclerosis that may impede successful reperfusion.[15,16]

In acute LVO stroke, most of the current randomized clinical trials failed to prove the noninferiority of MT alone versus IVT+MT.[1,3–5,17,18] In addition, recent meta-analyses have suggested a beneficial effect of IVT+MT over MT alone.[19,20] That said, the most recent guidelines from the European Stroke Organization-European Society for Minimally Invasive Neurological Therapy and Society of Vascular and Interventional Neurology still recommend that patients should receive IVT in addition to MT if eligible.[21,22] In TLs, recent pooled analyses including the TITAN (Thrombectomy in Tandem Lesions)

and Endovascular Treatment in Ischemic Stroke registries suggested that IVT before MT may increase the odds of favorable functional outcome without increasing the risk of hemorrhagic complications.[23] Moreover, results from the German Stroke Registry-Endovascular Treatment study showed that the use of IVT in TL was an independent predictor of successful reperfusion (modified Thrombolysis in Cerebral Infarction score of 2b-3) in patients treated with MT.[9]

Hence, in this study, we sought to evaluate the safety and efficacy of MT with or without IVT for patients presenting with acute TLs. In addition, we assessed whether the use of intraprocedural APT was associated with a greater risk of clinically relevant intracranial hemorrhage when added to IVT.

METHODS

Study Population

We used a pooled, multicenter cohort registry for the study. Patient eligibility and methods of collaboration have been reported previously.[24] Briefly, the study included adult patients with TL treated with MT within 24 hours after stroke onset from 16 stroke centers (15 hospitals in the United States and 1 in Spain) between January 2015 and December 2020. TL was defined as an intracranial LVO (petrous, sigmoid, or terminus segment of the internal carotid artery (ICA) or M1 or proximal M2 segment of the middle cerebral artery) with concomitant extracranial ICA stenosis ≥70% according to NASCET (North American Symptomatic Carotid Endarterectomy Trial).[25] Patients were divided into 2 groups: (1) IVT+MT group (patients treated with IVT before MT) and (2) MT alone group (patients who did not receive IVT before MT). Treatment with IVT was determined at the discretion of the treating clinician. All intracranial occlusions were treated using a stent-retriever and contact aspiration catheters. The endovascular and medical therapeutic interventions were performed according to the protocol of each institution under conscious sedation or general anesthesia and at the discretion of the neurointerventionalists. The study was approved under the waiver of informed consent by the local institutional review board at each participating center. This study follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) reporting guidelines (Supplemental Material).[26] Data will be available upon reasonable request.

We classified the intraprocedural APTs into 4 categories depending on the intraprocedural APT regimen used during MT: no intraprocedural APTs, single oral APTs (aspirin, clopidogrel, or ticagrelor), dual oral APT (aspirin+clopidogrel or aspirin+ticagrelor), or intravenous APT (IV-APT) with or without oral APT (GP IIb/IIIa [glycoprotein IIb/IIIa] inhibitor alone; IIb/IIIa and single oral; IIb/IIIa and dual oral; cangrelor and single oral; cangrelor and dual oral).

Outcome Measures

The primary outcomes of the study were symptomatic intracranial hemorrhage (sICH) and parenchymal hematoma type 2 (PH2). sICH was defined by the ECASS-3 (European Collaborative Acute Stroke Study) criteria as any type of intracranial hemorrhage on follow-

up imaging between 22 and 36 hours and 7 days after stroke onset and an increase of ≥4 points on the National Institutes of Health Stroke Scale from baseline or the lowest value within 7 days, or mortality.[27] The clinical evaluation was done by the stroke team at each site. We also assessed the rate of ischemic infarct hemorrhagic transformation (HT) defined as no hemorrhage, petechial hemorrhage (hemorrhagic infarction type 1 [H1] and type 2 [H2]), and parenchymal hematoma (parenchymal hematoma type 1 [PH1] and type 2 [PH2]), according to the Heidelberg Bleeding Classification.[28]

The secondary outcomes included successful (modified Thrombolysis in Cerebral Infarction 2b-3) or complete reperfusion (modified Thrombolysis in Cerebral Infarction 3), favorable functional outcome at discharge (discharge modified Rankin Scale score 0–2), favorable functional outcome at 90 days (90-day modified Rankin Scale score 0–2), excellent functional outcome at 90 days (90-day modified Rankin Scale score 0–1), in-hospital mortality, and mortality at 90 days.

Statistical Analysis

Descriptive statistics were used to summarize continuous and categorical variables. We reported counts and percentages for categorical variables and means (SD) or medians (interquartile range [IQR]) for continuous variables. Shapiro-Wilk test and histograms were used to assess the normality of distributions. For the univariable analysis, we used the Student *t* tests or Wilcoxon rank-sum test for continuous variables and χ^2 or Fisher exact test for categorical variables, as needed.

To evaluate the safety and efficacy outcomes between the 2 patient groups, we performed multivariable logistic regression. Details on the model selection, candidate variables, interaction terms, and subgroup analyses are presented in the Supplemental Methods. The odds ratios (ORs) and 95% CIs for the effect size of each group were computed. We also performed sensitivity analysis by time window within 0 to 6 hours from last known well (LKW)-to-arterial puncture (early window) for all the safety and efficacy outcomes and by type of admission on primary admission patients for favorable functional outcomes. The 6 hours cutoff point was selected with the goal to include a larger proportion of eligible patients for IVT according to the current guidelines.[29,30]

All the statistical analyses were considered significant at a 2-sided alpha level of ≤0.05. We used R statistical package (version 4.1.3, R Foundation for Statistical Computing, Vienna, Austria) for the analysis. Data will be made available upon reasonable request from the corresponding author.

RESULTS

Of the 691 patients from the registry, 179 were excluded (Figure 1). Of the 512 patients included, 218 were in the IVT+MT group, and 294 were in the MT alone group. The demographic data and baseline characteristics of the 2 groups are presented in the Table. Patients in the IVT+MT group had a lower rate of hypertension (67.9% versus 77.4%; *P*=0.016) and history of antiplatelet medications (28.7% versus 37.6%; *P*=0.037) than those in the MT alone group. Furthermore, patients in the IVT+MT group had a higher median

admission National Institutes of Health Stroke Scale (17 versus 15; *P*=0.034), a higher median Alberta Stroke Program Early Computed Tomography Score (9 versus 8; *P*=0.02), a lower median number of MT passes (1 versus 2; *P*=0.01), higher rate of first-pass effect (67.4% versus 55.5%; *P*=0.007), a lower median time from LKW-to-reperfusion (305 versus 662; *P*<0.001), and a lower median time from LKW-to-arterial puncture (245 versus 603 minutes; *P*<0.001) than those in the MT alone group. In addition, 323 (63.7%) patients underwent ICA stenting, 192 (65.8%) from the MT alone group, and 131 (60.9%) from the IVT+MT group (*P*=0.264). Finally, 259 (50.6%) patients were treated within the early window, with a higher proportion of patients treated in the early window receiving IVT (78.9% versus 29.6%; *P*<0.001).

Primary Outcomes

Compared with the MT alone group, the IVT+MT group had a higher rate of sICH, but this difference was not significant (7.8% versus 6.2%, *P*=0.470). After adjusting for the selected covariates, the difference in the risk of sICH between the 2 groups remained nonsignificant (unadjusted OR, 1.26 [95% CI, 0.63–2.53]; *P*=0.517; adjusted OR [aOR], 1.22 [95% CI, 0.60–2.51]; *P*=0.583; Figure 2A).

We assessed for any effect modification of the use of intraprocedural APT on the relationship between IVT and sICH by comparing models with and without an interaction term. This did not show a differential effect between patients who received intraprocedural APT and those who did not (x^2=5.66, df=3, *p*-het=0.129; Figure 3). However, when we explored this interaction by each intraprocedural APT category (Figure S1), a significant level was observed only in patients who received IV-APT ($P_{interaction}$=0.042; Table S1). In the sensitivity analysis, IVT increased the risk of sICH in patients treated with IV-APT therapy (aOR, 3.04 [95% CI, 0.99–9.37]; *P*=0.05). The effect of IV-APT on the increased risk of sICH with IVT appears related to the use of GP IIb/IIIa inhibitors (Figure S2).

There were no significant differences in the rates of PH2 between the 2 groups (IVT+MT: 6.4% versus MT alone: 7.1%, *P*=0.749). After adjusting for confounders, the difference remained nonsignificant (unadjusted OR, 0.89 [95% CI, 0.44–1.80]; *P*=0.749; aOR, 0.99 [95% CI, 0.47–2.08]; *P*=0.985; Figure 2A). The comparison between the models with and without an interaction term to assess the effect of intraprocedural APT on the relationship between PH2 and IVT showed no differential effects (x^2=3.58, df=3, *p*-het=0.31). In addition, the interaction by each intraprocedural APT category was also nonsignificant (Figure S3; Table S2). In the sensitivity analysis, the use of IVT did not increase the risk of PH2 with any of the intraprocedural APTs.

With respect to HT, the risk was not significantly different between the MT alone and the IVT+MT groups (aOR, 0.95 [95% CI, 0.62–1.46]; *P*=0.817; Figure S4). The interaction evaluation showed no significant effect between intraprocedural APT and IVT for HT (IVT×dual oral APT *P*nteraction=0.189; IVT×single oral APT *P*nterac$_{tion}$=0.264; IVT×IV-APT $P_{interaction}$=0.681). In the sensitivity analyses, the use of IVT did not increase the risk of HT with any of the intraprocedural APTs.

Secondary Outcomes

At 90 days, there was a higher, albeit not statistically significant, rate of favorable functional outcome in the IVT+MT group compared with the MT alone group (48% versus 44.7%, P=0.481). After adjusting for covariates, the IVT+MT group had higher odds of a favorable functional outcome (unadjusted OR, 1.75 [95% CI, 1.02–2.18]; P=0.043; aOR, 1.72 [95% CI, 1.01–2.91]; P=0.045; Figure 4A). In addition, we observed a trend toward increased odds of a favorable outcome in primary admission patients treated with IVT (aOR, 1.84 [95% CI, 0.97–3.55]; P=0.06). In subgroup analyses, there was heterogeneity across intraprocedural APTs and ICA stenting, with stronger odds of favorable outcomes in patients treated with ICA stenting and in those treated with dual oral APTs (Figure 5).

The odds of successful reperfusion (aOR, 0.95 [95% CI, 0.47–1.93]; P=0.895) and excellent reperfusion (aOR, 0.72 [95% CI, 0.46–1.12]; P=0.141) were not different between patients treated with IVT+MT versus MT alone (Table S3). There was no significant interaction between intraprocedural APT and IVT for successful reperfusion ($P_{\text{interaction}}$=0.232); however, there was a significant interaction between IV-APT use with IVT for the outcome of excellent reperfusion ($P_{\text{nteraction}}$=0.019). In the sensitivity analysis, the use of IVT did not increase the odds of achieving excellent reperfusion with any of the intraprocedural APTs.

In the multivariable analysis, no association was found for in-hospital mortality (aOR, 0.99 [95% CI, 0.44–2.21]; P=0.977) and 90-day mortality (aOR, 0.98 [95% CI, 0.44–2.18]; P=0.956) with the use of IVT prior MT (Table S3).

Early Window Sensitivity Analysis

The early window included only patients with LKW-to-arterial puncture time <6 hours. Similar to the primary analysis, we found no significant differences in the rates of sICH (aOR, 1.70 [95% CI, 0.52–5.60]; P=0.381), PH2 (aOR, 0.93 [95% CI, 0.32–2.67]; P=0.894; Figure 2B), and HT (aOR, 1.33 [95% CI, 0.70–2.52]; P=0.382). The IVT+MT group showed greater odds of a favorable functional outcome at 90 days (aOR, 1.97 [95% CI, 1.04–3.80]; P=0.039; Figure 4B). Finally, there were no differences in additional outcomes (Table S3).

DISCUSSION

Our study compared the safety and efficacy of IVT+MT versus MT alone in patients presenting with acute TLs. We found that (1) the administration of IVT before MT was safe and was not associated with an increased risk of sICH, PH2, or HT; (2) treatment with IVT plus MT was associated with a higher rate of favorable functional outcome at 90 days, especially in TL-patients treated within the 6-hour time window; and (3) the use of intraprocedural IV-APT was associated with an increased risk of sICH in patients who received IVT, but this did not translate into worse clinical outcomes (Figure 5).

The role of IVT in patients with LVO stroke eligible for MT has been a subject of debate. Theoretically, adding IVT may contribute to achieving early reperfusion of the ischemic territory before MT,[16,31–33] increase reperfusion rates with fewer recanalization attempts,[34] and may improve outcomes in patients with failed MT reperfusion attempts.[35] However, the theoretical risk of distal clot embolization to locations not amenable to MT[36] and

intracranial hemorrhage, the potential delays for arterial puncture, and its elevated cost are considerable disadvantages.[37,38]

TLs are often excluded and, therefore, underrepresented in clinical trials. As a result, the level of evidence to evaluate the safety of the use of IVT+MT is limited. A pooled analysis of the TITAN and Endovascular Treatment in Ischemic Stroke registries found that bridging therapy did not increase the risk of sICH or PH2, as per our findings.[23] They reported a rate of 7.5% for sICH and 5.6% for PH2 in their IVT+MT group, which is comparable with our 7.8% rate for sICH and 6.4% for PH2. Furthermore, our rate of sICH was similar to the rates reported in the 6 randomized clinical trials of bridging therapy in acute LVO, which ranged from 4.7% to 7.8%.[1,3–5,17,18] In our study, we also found that the IVT+MT did not increase the risk of HT, which is relevant considering that IVT may promote HT through fibrinolytic and immune mechanisms.[39] This finding was consistent in our population independently of the underlying cause, baseline Alberta Stroke Program Early Computed Tomography Score, use of stenting, complete cervical occlusion, or presentation time.

APT has been reported safe, with a low risk for intracranial hemorrhage in patients with TL.[14] Its administration primarily occurs intraprocedural to prevent an acute in-stent thrombosis and subsequent restenosis of the cervical segment when a cervical ICA stenting is pursued.[40] Zhu et al[13] found that IVT before MT did not lead to a significant association with APT (aspirin, clopidogrel, or glycoprotein IIb/IIIa receptor antagonist) and hemorrhagic and procedural complications in patients with TL. Similarly, Anadani et al did not find evidence of heterogeneity in treatment effect sizes according to prior IVT for the risk of hemorrhagic complications. They concluded that ICA stenting was safe in patients with previous IVT.[7] According to the ARTIS trial (Antiplatelet Therapy in Combination With rt-PA Thrombolysis in Ischemic Stroke) results, early therapy with intravenous aspirin may increase the risk of hemorrhagic complications in patients who have already received IVT.[41] Nevertheless, high-level data are required to guide management decisions regarding the use of intraprocedural APTs and cervical ICA stenting. Currently, 2 ongoing randomized clinical trials (TITAN trial [https://www.clinicaltrials.gov; Unique identifier: NCT03978988]; EASI-TOC trial [Endovascular Acute Stroke Intervention - Tandem Occlusion Trial; https://www.clinicaltrials.gov; Unique identifier: NCT04261478]) aim to assess the safety and efficacy of ICA stenting using different antiplatelet regimens, which will provide us with important insight into the safety of periprocedural antiplatelets.

In our study, we did not find an overall IVT-by-intraprocedural APT interaction. However, when we explored the independent interaction at each of the APT categories, we found that intraprocedural IV-APT (which included GP IIb/IIIa inhibitors and cangrelor) seemed to increase the risk of sICH in patients treated with IVT+MT. Similarly, Stampfl et al[42] attributed the high ICH rate (16.6%) to intravenous APT with tirofiban, considering that most of their patients (92%) were treated with IVT before ICA stenting. Also, Heck and Brown found that intravenous APT with abciximab after acute ICA stenting may be associated with higher rates of sICH (31%) in TLs,[43] and 1 matched cohort analysis reported a higher rate of parenchymal hemorrhage in patients with TLs and those concomitantly treated with eptifibatide.[44] The ATILA project (Aspirin Versus Tirofiban in Endovascular Treatment for Patients With Acute Ischemic Stroke due to Tandem Lesion project;

NCT05225961) is a multicenter phase IV randomized clinical trial aimed at determining the safety and efficacy of intravenous tirofiban versus intravenous aspirin in patients with TL treated with MT. The results of this trial will be helpful in understanding the safety of tirofiban in TL. In addition, we observed that the use of GP IIb/IIIa inhibitors was associated with all the hemorrhage cases related to IVT compared with cangrelor (Figure S1). However, the small sample sizes in these subgroups are a limitation for drawing a definite conclusion.

We did not find an association between the use of IVT and successful reperfusion when evaluating our entire TL population. These results are in contrast with the recently published literature that evaluated TL presenting within 8 hours after symptom onset.[23] However, when evaluating patients in the early window after adjusting for confounders, IVT was associated with higher odds of functional independence at 90 days. Interestingly, the different effects of IVT on successful reperfusion and functional independence reflect the heterogeneity and chronicity of the occlusions, which may introduce further complexity in the treatment of TLs due to collateral circulation. More importantly, the advantages of pretreatment with IVT, such as clot decomposition and recanalization of microvasculature, might have an additional beneficial effect independently of proximal vessel recanalization.[45] In fact, the recently reported CHOICE trial (Chemical Optimization of Cerebral Embolectomy) has shown that the addition of intra-arterial tissue-type plasminogen activator was associated with better functional outcomes at 90 days without any significant differences in the rates of reperfusion or sICH.[46]

This study has several limitations. First, there is a potential selection bias due to the retrospective nature of its design. Second, the patient selection was determined according to the clinical evaluation of each center and neuro-interventionalist and, therefore, lacks randomization. Third, the clinical and imaging data were self-adjudicated by independent investigators at each center without external control or core imaging laboratory adjudication. Fourth, relevant safety outcomes such as postprocedural and 24-hour extracranial stent patency were not available and, therefore, we could not assess the role of the APT regimen during (and after) MT in-stent patency. Fifth, the significant results from our interaction analysis must be interpreted with caution due to the fact that the overall interaction term (*p*-het) was not significant, the small number of events in each APT category, and the potential lack of power of the tests. Finally, the predictive models should be interpreted with caution considering the limited sample size and the potential risk of confounding by measured and unmeasured variables.

CONCLUSIONS

Our study shows that IVT+MT for TL cases did not increase the overall risk of sICH, PH2, or overall HT independently of the cervical revascularization technique used. However, the use of intraprocedural IV-APT during stent implantation may be associated with an increased risk of sICH in patients who received IVT before MT. Importantly, treatment with IVT+MT was associated with a higher rate of favorable functional outcomes at 90 days, especially in patients within the 6-hour window. Prospective studies are warranted for confirmation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Nonstandard Abbreviations and Acronyms

aOR	adjusted odds ratio
APT	antiplatelet therapy
ECASS-3	European Collaborative Acute Stroke Study
HT	hemorrhagic transformation
ICA	internal carotid artery
IQR	interquartile range
IVT	intravenous thrombolysis
LVO	large-vessel occlusion
MT	mechanical thrombectomy
NASCET	North American Symptomatic Carotid Endarterectomy Trial
PH2	parenchymal hematoma type 2
sICH	symptomatic intracranial hemorrhage
TITAN	Thrombectomy in Tandem Lesions
TL	tandem lesion

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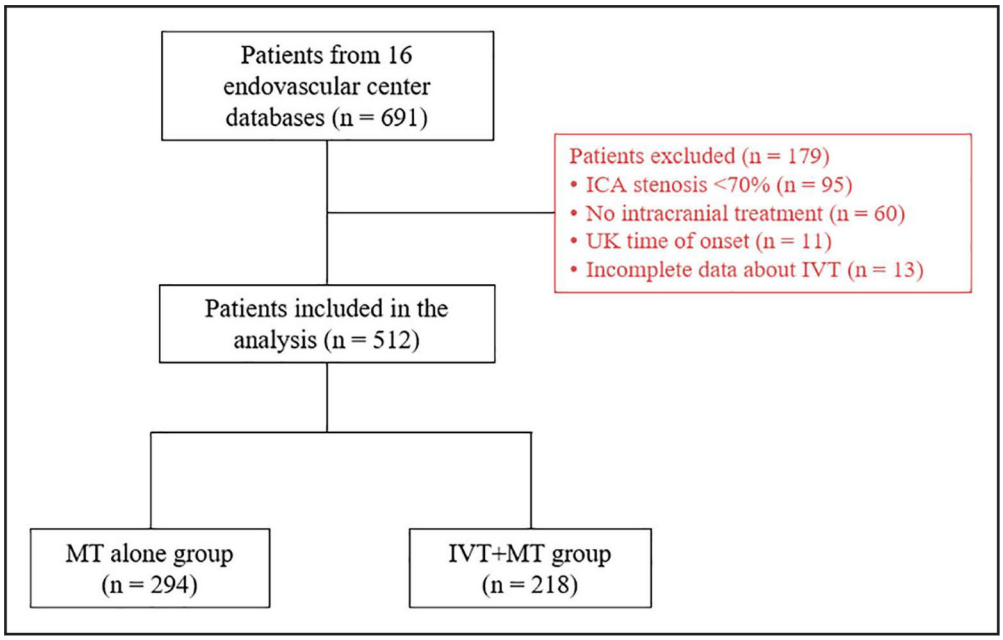

Figure 1. Flow diagram of patients included in the study.

ICA indicates internal carotid artery; IVT, intravenous thrombolysis; LKW, last known well; MT, mechanical thrombectomy; and UK, unknown.

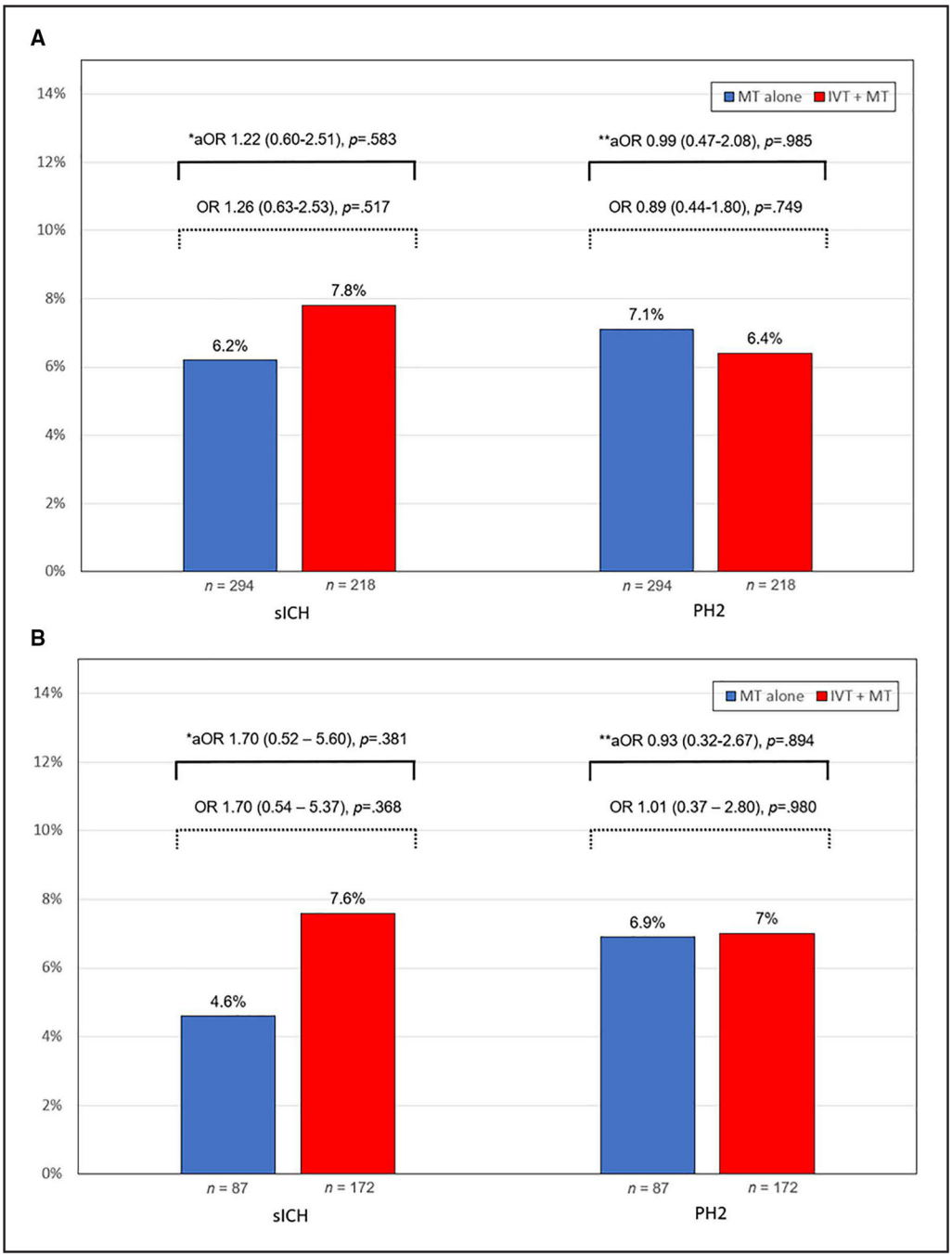

Figure 2. Symptomatic intracranial hemorrhage (sICH) and parenchymal hematoma type 2 (PH2) in patients treated with mechanical thrombectomy (MT) alone and intravenous thrombolysis (IVT)+MT.

Bar chart illustrating the results for the primary analysis (**A**) and the sensitivity analysis for the early window (0–6 hours; **B**). *Adjusted for internal carotid artery (ICA) stenting, number of passes, modified Thrombolysis in Cerebral Infarction 2b-3. **Adjusted for ICA stenting, age, hypertension, Alberta Stroke Program Early Computed Tomography Score.

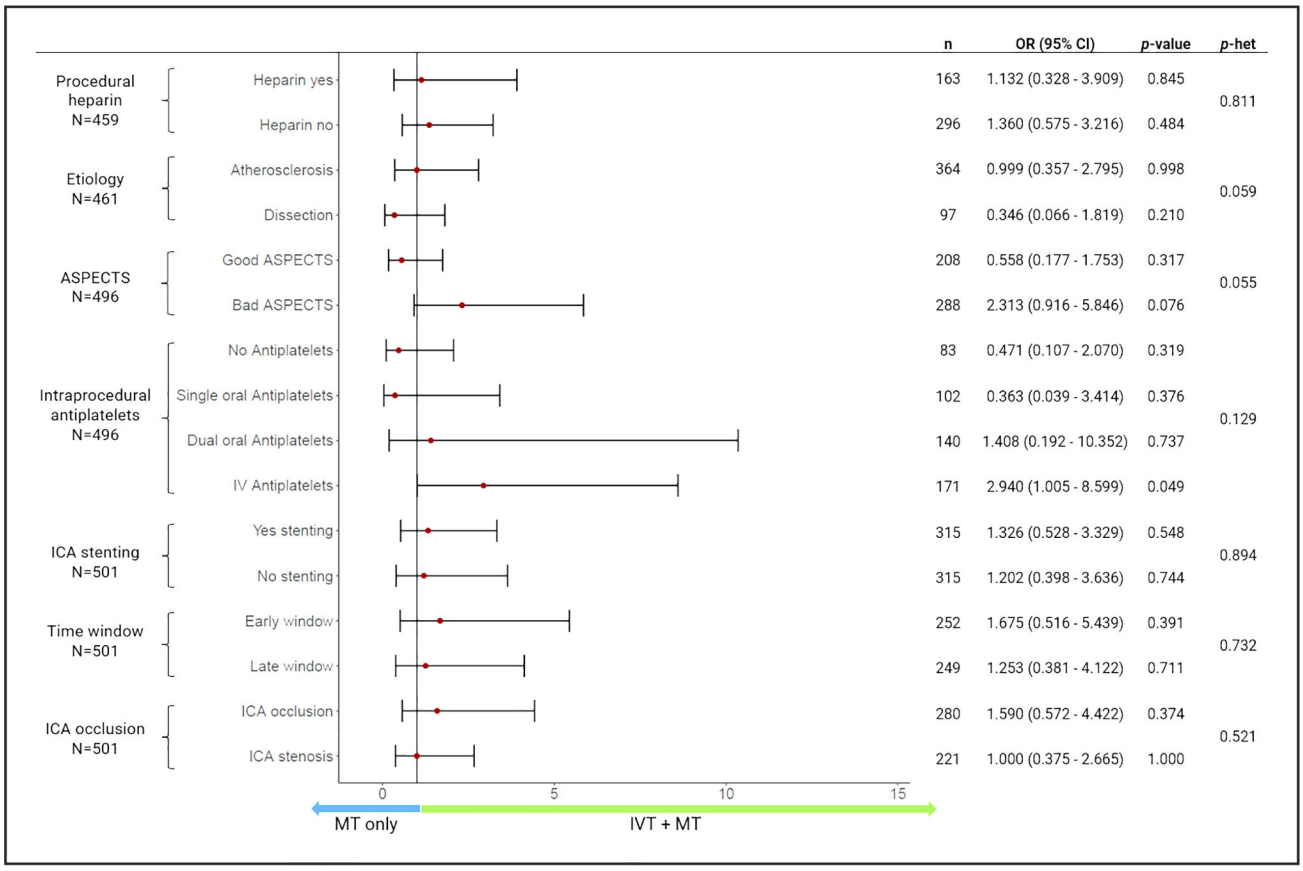

Figure 3. Comparisons in symptomatic intracranial hemorrhage according to the use of intravenous thrombolysis (IVT) in prespecified subgroups.

Adjusted for number of passes, modified Thrombolysis in Cerebral Infarction. *p*-het: *P* value for test of interactions. ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; ICA, internal carotid artery; MT, mechanical thrombectomy; OR, odds ratio for sICH; and *p*-het, *P* value of heterogeneity.

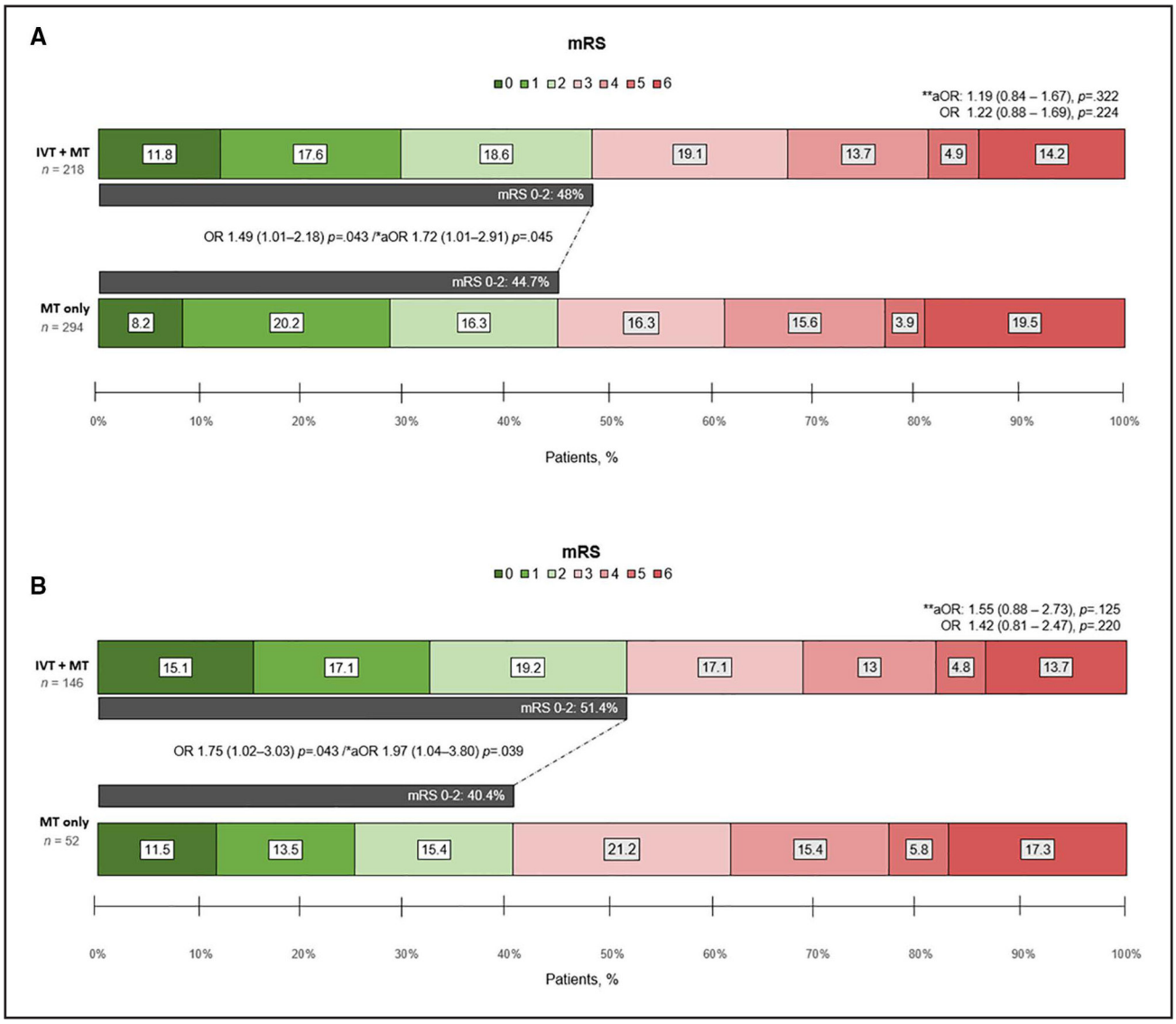

Figure 4. Shift analysis of modified Rankin Scale (mRS) at 90 days in patients treated with mechanical thrombectomy (MT) alone and intravenous thrombolysis (IVT)+MT.

Bar chart depicting the results of the entire cohort (**A**) and the sensitivity analysis for the early window (0–6 hours; **B**). aOR indicates adjusted odds ratio; IVT, intravenous thrombolysis; MT, mechanical thrombectomy; and OR, odds ratio. *Categorized mRS score 0 to 2 vs 3 to 6. Adjusted for age, National Institutes of Health Stroke Scale (NIHSS), type of anesthesia, successful reperfusion, internal carotid artery stenting, symptomatic intracranial hemorrhage, and postprocedural antiplatelet therapy. **Multinomial model. Adjusted for age, NIHSS, type of anesthesia, successful reperfusion, internal carotid artery stenting, symptomatic intracranial hemorrhage, and postprocedural antiplatelet therapy.

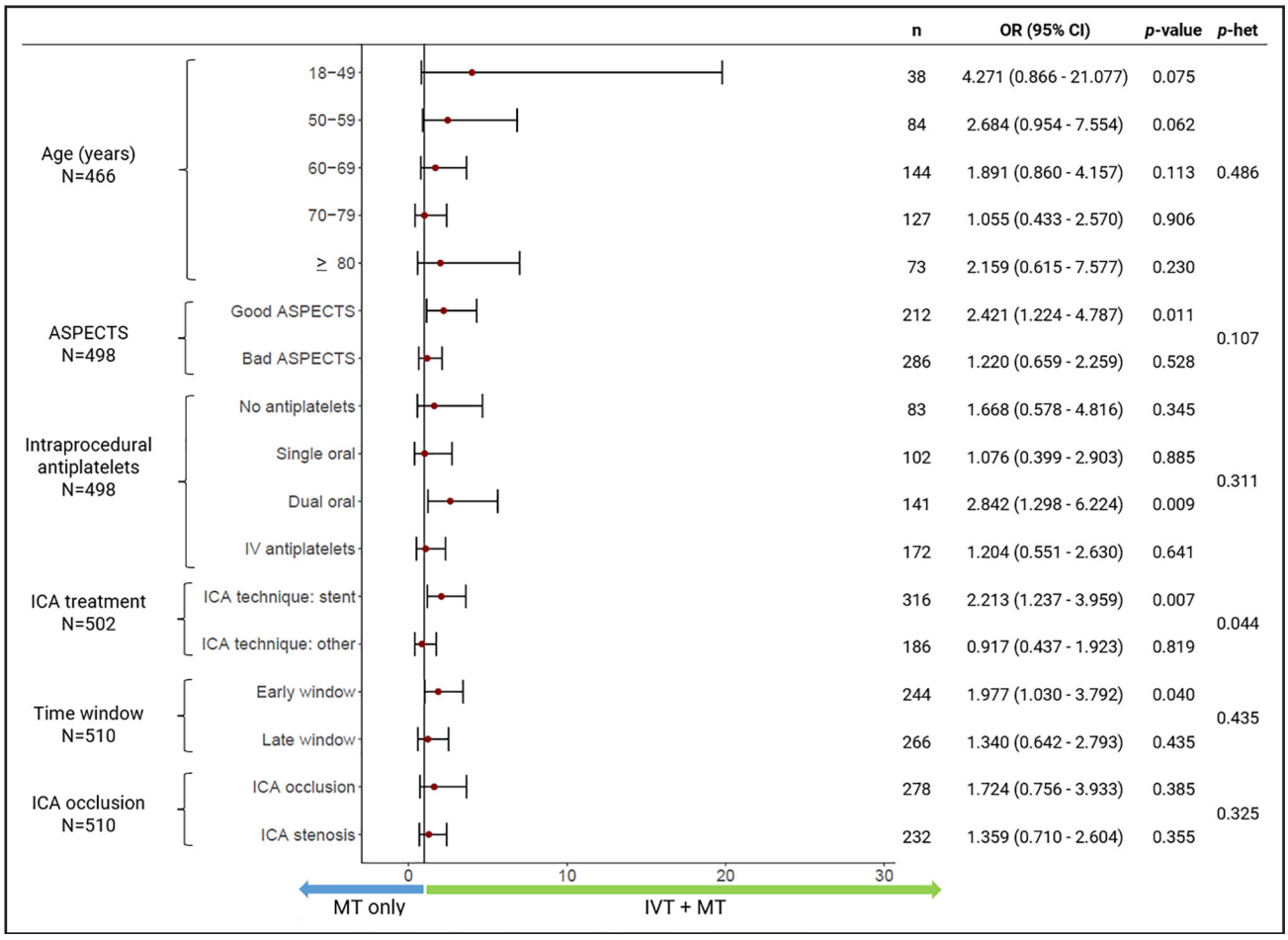

Figure 5. Comparisons of favorable outcomes at 90 days according to the use of intravenous thrombolysis (IVT) in prespecified subgroups.

ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; ICA, internal carotid artery; MT, mechanical thrombectomy; OR, odds ratio of favorable outcome at 90 days; and *p*-het, *P* value of heterogeneity.

Table.

Baseline and Treatment Characteristics of Patients With Endovascularly Treated Tandem Lesions According to the Use of Intravenous Thrombolysis

	Total (N=512)	**MT alone (N=294)**	**IVT+MT (N=218)**	***P* value**
Age, y; median (IQR)	68 (59–76)	68 (61–75.7)	66 (58–75.8)	0.113
Females, N (%)	154 (30.1)	91 (31)	63 (28.9)	0.616
White race, N (%)	322 (63.4)	186 (64.1)	136 (62.4)	0.685
Medical history, N (%)				
Hypertension	374 (73.3)	226 (77.4)	148 (67.9)	0.016 *
Hyperlipidemia	229 (45.1)	138 (47.4)	91 (41.9)	0.219
Diabetes	137 (26.9)	82 (28.1)	55 (25.3)	0.491
Atrial fibrillation	63 (12.4)	43 (14.7)	20 (9.2)	0.062
Current smoker	118 (23.3)	69 (24)	49 (22.5)	0.891
Previous stroke/TIA	77 (15.1)	49 (16.8)	28 (12.9)	0.227
Coronary artery disease	96 (18.8)	60 (20.5)	36 (16.5)	0.257
Prior antiplatelets, N (%)	171 (33.8)	109 (37.6)	62 (28.7)	0.037 *
Transfer from outside institution, N (%)	279 (55.7)	156 (54.7)	123 (56.9)	0.622
Admission glucose (mg/dL), median (IQR)	125 (107–154)	125 (107–153)	125 (107–154)	0.691
Baseline mRS, N (%)				0.708
0	401 (80)	230 (79.6)	171 (80.7)	
1	39 (7.8)	21 (7.3)	18 (8.5)	
2	35 (7)	21 (7.3)	14 (6.6)	
3	20 (4)	14 (4.8)	6 (2.8)	
4	5 (1)	2 (0.7)	3 (1.4)	
5	1 (0.2)	1 (0.3)	0 (0)	
Admission NIHSS, median (IQR)	16 (11–20)	15 (10–20)	17 (12–20)	0.034 *
ASPECTS, median (IQR)	8 (7–9)	8 (7–9)	9 (7–10)	0.002 *
Cervical ICA lesion cause, N (%)				0.201
Atherosclerosis	402 (78.8)	236 (80.8)	166 (76.1)	
Dissection	52 (10.2)	28 (9.5)	24 (11)	

	Total (N=512)	MT alone (N=294)	IVT+MT (N=218)	*P* value
Other [†]	56 (10.9)	28 (9.5)	28 (12.8)	
Intracranial occlusion location, N (%)				0.063
ICA	87 (27.2)	58 (30.9)	29 (22)	
M1	187 (58.4)	109 (58)	78 (59.1)	
M2	46 (14.4)	21 (11.2)	25 (18.9)	
Cervical ICA complete occlusion, N (%)	280 (54.7)	167 (56.8)	113 (51.8)	0.264
General anesthesia, N (%)	203 (39.6)	118 (40.1)	85 (39)	0.793
First-line technique, N (%)				0.379
Combination	267 (53.3)	149 (51.7)	118 (55.4)	
Aspiration device	150 (29.9)	85 (29.5)	65 (30.5)	
Stent-retriever	84 (16.8)	54 (18.8)	30 (14.1)	
IA tPA, N (%)	18 (3.6)	10 (3.5)	8 (3.8)	0.884
Number of passes, median (IQR)	2 (1–3)	2 (1–3)	1 (1–2.5))	0.001 [*]
First-pass effect, N (%)	301 (60.7)	156 (55.5)	145 (67.4)	0.007 [*],
ICA stenting, N (%)	323 (63.7)	192 (65.8)	131 (60.9)	0.264
Intraprocedural heparin, N (%)	183 (35.7)	104 (35.4)	79 (36.2)	0.840
Intraprocedural antiplatelets. N (%)				0.152
Dual oral	148 (28.9)	87 (29.6)	61 (28)	
Any intravenous	173 (33.8)	107 (36.4)	66 (30.3)	
None	87 (17)	41 (13.9)	46 (21.1)	
Single oral	104 (20.3)	59 (20.1)	45 (20.6)	
Time metrics, median (IQR)				
LKW-to-reperfusion, min	447 (286–765)	662 (422–978)	305 (228–404)	<0.001 [*]
LKW-to-arterial puncture, min	375 (217–706)	603 (356–904)	245 (168–349)	<0.001 [*]
Window, N (%)				<0.001 [*]
Early	259 (50.6)	87 (29.6)	172 (78.9)	
Late	226 (44.1)	182 (66.2)	44 (20.2)	
Very late	27 (5.3)	25 (8.5)	2 (0.9)	

ASPECTS indicates Alberta Stroke Program Early Computed Tomography Score; IA tPA, intra-arterial tissue-type plasminogen activator; ICA, internal carotid artery; IQR, interquartile range; IVT, intravenous thrombolysis; LKW, last known well; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; and TIA, transitory ischemic attack.

[*] *P* value<0.05.

[†] No dissection or plaque was found after ICA occlusion was revascularized.