Clinical Results of the ANAIS study: Mechanical thrombectomy using the ANA device in combination with a stent retriever in subjects with Acute Ischemic Stroke

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Abstract

Background and Purpose: The ANA Mechanical Thrombectomy (Anaconda Biomed, Barcelona) is a funnel catheter comprised of a self-expanding coated funnel, works in conjunction with a standard stentretriever, and is designed to locally restrict flow and reduce clot fragmentation. The ANAIS Study investigated the performance of the ANA funnel catheter in stroke patients.

Materials and Methods: Prospective, single-arm, multi-center study with blinded outcomes assessment by independent imaging core lab. Patients with anterior circulation stroke undergoing mechanical thrombectomy were eligible. Primary endpoint was successful reperfusion (eTICI2b50-3) within three passes without rescue therapy. Safety endpoint combined symptomatic intracranial hemorrhage and severe adverse device effect .

Results: 43 subjects were treated in 3 centers: mean age: 70.5±13.1 years, 44.2% (19/43) female median admission National Institutes of Health Stroke Scale 16.0 [12.5-19.5].

Primary endpoint was achieved in 70% (30/43) and 81% (26/32) in the intention-to-treat (ITT) and per-protocol (PP) populations, respectively. The rates of first pass eTICI 2c-3 were 44% (19/43) and 56% (18/32) in the ITT and PP populations, respectively. There were no SADE/sICH at 24 hours (0/43). When the funnel was deployed in the C1 segment of the (Bouthillier Classification) the primary endpoint (ITT: 36%; PP: 57%) was lower than when deployed in the C2/C3 segments (ITT: 89%; PP:100%; $p < 0.01$), or in the C4

segment or above segments (ITT:71%; PP:77%; $p < 0.05$). Primary endpoint was higher when continuous aspiration was applied from initiation of retrieval maneuver (ITT:81%; PP:92%) as compared to end aspiration only (ITT 36%; PP:50%, $p < 0.01$).

Conclusions: The ANA funnel catheter achieved high rates of reperfusion and first pass success, with a good safety profile. Successful reperfusion was higher superior when the funnel was deployed above the C1 segment of internal carotid artery and clot retrieval conducted under continuous aspiration.

Abbreviations

eTICI=Expanded treatment in cerebral infarction; ICA=internal carotid artery; ICH=intracranial hemorrhage; ITT=intention-to-treat; mRS=modified Rankin Scale; MT=Mechanical Thrombectomy; NIHSS=National institutes of Health Stroke Scale; PP=per-protocol; SADE= Severe adverse device effect ; SR=stent retriever.

Disclosure of potential conflicts of interest

BLINDED FOR PEER REVIEW.

Introduction

Mechanical thrombectomy (MT) is the most effective treatment for acute ischemic stroke due to large vessel occlusion when combined with IV-tPA, unless contraindicated, and is currently strongly recommended by all clinical guidelines[1, 2].

Common metrics associated with the success of the procedure, including the time from onset of symptoms to reperfusion[3], and complete reperfusion in a minimum number of attempts[4] without distal clot fragmentation, are strongly associated with the clinical outcome of the patient[5]. For this reason, there is a continuous effort to develop new treatment strategies and advanced devices to improve the performance of the procedure[6]. The ANA funnel catheter device (Anaconda Biomed S.L. in Barcelona, Spain) represents an innovative stroke thrombectomy tool. The ANA funnel catheter is designed to facilitate the delivery of stent retrievers during MT and create flow arrest and reversal during clot retrieval. The funnel, when deployed, allows for simultaneous aspiration and may improve clot ingestion, thus limiting the risk for fragmentation of the thrombus. Once the clot is positioned inside the funnel, the SR and ANA funnel catheter are simultaneously retrieved into the guiding catheter to extract the clot.

In both in-vitro phantom experiments and swine models simulating human neurovascular anatomy, the ANA funnel catheter demonstrated higher reperfusion rates compared to SR used alongside a distal aspiration catheter or a balloon guiding catheter [7, 8].

First in human trials of the initial iteration of the ANA funnel catheter have shown promising results regarding safety and efficacy[9,10]. Recently, the device has been redesigned to be readily deployed at the level of intracranial carotid artery, and the

delivery catheter has been eliminated, leading to an easier-to-use version of the device, deliverable through any guiding catheter, in which the funnel concept and its potential advantages restricting flow and facilitating clot ingestion are maintained.

This study aims to evaluate the efficacy, safety, and performance of the ANA funnel catheter and how these results can be influenced by funnel positioning or aspiration methods in a prospective in vivo study.

Materials and Methods

Study Design

The ANAIS Study was a prospective, single-arm, multi-center study aiming to confirm the safety and performance of the ANAfunnel catheter , in combination with a stent retriever in subjects with AIS with blinded assessment of the outcomes by an independent imaging core lab and a clinical event committee (CEC). The investigational use of the ANA funnel catheter and the clinical protocol were approved by the national regulatory agency and the Institutional Ethics Committee (STUDY number ANA2201 Acta n 24 25/03/2022). Informed consent to participate in the trial was obtained from all patients or their next of kin before treatment. Patients did not receive any compensation for participating in this study.

The STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) reporting guidelines were used to generate the manuscript.

Description of ANA Funnel Catheter and Procedure

Details of the device have been previously described[9].

During the procedure, the ANA funnel catheter is initially positioned in its retracted state inside the guiding catheter. After advancing the microcatheter through the occlusion site and deploying the Solitaire family stent retriever (SR) as per usual practice, the funnel is deployed to locally restrict flow. The funnel self-expands to the diameter of the artery. Subsequently, the microcatheter is completely withdrawn to enlarge the aspiration lumen. The SR is then retrieved, and manual aspiration is applied through the ANA funnel catheter. Once the distal ends of the SR and ANA funnel catheter are aligned, both are simultaneously pulled out.

Participants

Consecutive patients aged 18 to 85 years with anterior circulation vessel occlusion (including terminal ICA, M1-MCA, and M2-MCA) admitted within 24 hours from symptom onset, with a pre-stroke modified Rankin Scale (mRS) score of 0–1, and an Alberta Stroke Program Early CT Score >5 were eligible. (The full list of inclusion and exclusion criteria is included in the Supplemental Material Table 1). Thrombectomy with the ANA funnel catheter was attempted in all participants. Although the ANA funnel catheter is compatible with most commercially available stent retrievers, to minimize variability and facilitate comparisons with previously published series, neurointerventionalists were instructed to use stent retrievers from the Solitaire (Medtronic) family.

Out of the initial intention-to-treat (ITT) cohort, 11 patients were excluded for the per protocol (PP) analysis for the following reasons: four due to a finding of intracranial atherosclerotic disease (ICAD), two related to unstable guide catheter placement, and five for multiple minor deviations or insufficient ANA funnel catheter passes, culminating in a PP population of N=32 (See Figure 2 Flow-chart)

Efficacy outcome

The primary efficacy endpoint was successful reperfusion, defined as achieving eTICI 2b50-3 in the target vessel within three passes of the ANA funnel catheter without the use of rescue therapy, as assessed by the Core Lab. The CoreLab evaluated the eTICI considering the eTICI 2b50 in the results include eTICI 2b50 and eTICI 2b67; the minimum is eTICI 2b50. Therefore the endpoint eTICI 2b-3 is considered form the eTICI 2b50 to the eTICI3.

Rescue therapy was defined as any thrombectomy attempt not using the ANA funnel catheter.

Secondary efficacy endpoints included eTICI score after first pass and at the end of the procedure, procedural time (defined as time from puncture to achievement of eTICI 2b50-3, or if not achieved, to the final angiogram), thrombectomy time (defined as time from first baseline angiogram to achievement of eTICI 2b50-3, or, if not achieved, to the final angiogram), neurological status at Day 5 (± 12 hours) or discharge (whichever came first, determined by National institutes of Health Stroke Scale (NIHSS) score and favorable outcome at 90±14 days defined as modified Rankin Scale (mRS) score 0-2.

Safety outcome

The Clinical Events Committee reviewed all adverse events to determine their severity, seriousness (Serious Adverse Events) and to adjudicate causality related to the procedure or the device. The primary safety endpoint was a composite of symptomatic Intracranial Hemorrhage (symptomatic ICH) within 24 hours (-8/+12 h) post-procedure together with serious adverse device-related effects (SADE) at day 5 or discharge (SADE,.i.e. arterial

perforation or dissection during the procedure in relation to the use of the investigational device.

The presence of intracranial hemorrhage (ICH) on 24 hours CT was considered symptomatic when associated with clinical deterioration (worsening NIHSS score of ≥4 points) or led to death and was identified as the predominant cause of the neurological deterioration, as adjudicated by the Clinical Event Committee.

Secondary safety endpoints were occurrence of ICH, procedure-related mortality rate at day 5 (± 12 hours) or discharge, whichever came first, and at 90 days, occurrence of procedural complications: embolization in a previously uninvolved territory on the cerebral angiogram, arterial perforation, arterial dissection and vasospasm in the target vessel.

Statistical analysis

Using the IBM SPSS Statistics 25.0 software, descriptive and frequency-based statistical analyses and comparisons were carried out. The Kolmogorov-Smirnov test was used to determine if variables were normally distributed. Results were expressed as mean ± standard deviation or median ± interquartile range, as appropriate.

The effect of the funnel location on the ICA segments (ranging from segments C1 to C4 and above) and the impact of concurrent aspiration application on the angiographical outcome were also evaluated with a Z test for two proportions.

Additional performance analyses

We studied the impact of the funnel deployment location (according to the Bouthillier classification) on the reperfusion outcomes. We also analyzed the differences in efficacy when aspiration was applied from the beginning of the SR retraction compared to aspiration applied only in the last step when the SR is pulled into the funnel.

Results

Baseline Characteristics of the ITT and PP Populations

We enrolled 43 consecutive patients in 3 comprehensive stroke centers. Baseline characteristics are shown in Table 1.

In the ITT population, the average age of participants was 70.5 years (± 13.1y), with 44.2% (19/43) being female. Baseline characteristics of the ITT and PP populations are shown on Table 1.-There were 10 different interventionalists with a median of 3.0 cases per interventionalist (IQR 1.3- 6.5).

Safety Outcomes

In the Intent To Treat (ITT) population (n=43), the rate of combined symptomatic intracerebral hemorrhage (ICH) or death within 24 hours post-procedure was 0%. However, about 14.6% (6/43) of patients experienced neurological deterioration within the first 24 hours (unrelated to the procedure or the device per clinical event committee adjudication). There were no serious adverse device-related effects (SADE) within the first 5 days. At the 90-days, the all-cause mortality rate was 14.0% (6/43). Within the first 24 hours, 40.5% of patients (17/43) had an asymptomatic intracranial hemorrhage, as assessed by the Core Lab, of which 16.3% (7/43) had a subarachnoid hemorrhage , and 16.3% (7/43) had an HI-1 level hemorrhage. A smaller percentage, 9.5% (4/43), experienced an HI-2 level hemorrhage.

There were no Procedural Complications (including no embolization in new territory, vessel dissection, vessel perforation or vasospasm: 0%).

A total of 23 serious adverse events (SAE) occurred at 90 day. None of them were related to the procedure or the device according to the CEC. The most common were aspiration pneumonia (4/43), malignant stroke (2/43) and recurrent stroke (2/43).

Two Adverse Events were adjudicated to be related to the procedure or/and the device: a distal embolization was adjudicated by the Clinical Event Committee as "probably related to the procedure, and possibly related to the ANA funnel catheter". A thrombosis around the ANA catheter was adjudicated by the Clinical Event Committee as "possibly related to the procedure, and possibly related to the ANA device", and the most probable cause was inadequate flushing of the system. This adverse event was also reported as a device deficiency.

Safety Outcomes are shown in Table 2, A, and a list of all reported SAEs and AEs by the local investigators is available in the supplemental material.

Efficacy Outcomes

Efficacy Outcomes are shown in Table 2, B.

The primary efficacy endpoint, defined as successful reperfusion (eTICI 2b50-3) within 3 ANA passes without rescue therapy, was achieved in 70% of ITT and 81% of PP populations.

Secondary efficacy endpoints revealed complete reperfusion (eTICI 2c-3) within 3 ANA passes in 54% of ITT and 66% of PP patients.

First pass success rates (eTICI 2b50-3) were 51% in ITT and 66% in PP and rates of "near-complete" first pass reperfusion r (eTICI 2c-3) were 44% in ITT and 56% in PP. Results achieved when the results were narrowed to eTICI 3 are reported in Table 3.

The final successful reperfusion rate (eTICI 2b50-3) was 95% for ITT and 97% for PP.

The average median number of passes to achieve eTICI 2b50-3 was 1.0 (IQR 1.0, 2.0) in ITT and 1.0 (IQR 1.0, 1.5) in PP. The mean procedure time was 56.1 ± 38.0 minutes for ITT and 44.3 ± 27.6 minutes for PP, while the mean thrombectomy time was 46.8 ± 36.6 minutes for ITT and 35.7 ± 25.7 minutes for PP.

Neurological function, measured by NIHSS score at day 5 or discharge, showed a median of 3 [1-19] for the ITT, and 3 [1.0-14] for the PP.

At 90 days, 52.4% (22/42) and 55.2% (17/31) of patients achieved an mRS score between 0 and 2 in the ITT and PP populations, respectively. Furthermore, an mRS score of 0-1, denoting an excellent clinical outcome, was attained by 38.1% (16/42) and 45.8% (14/31) of subjects in the ITT and PP populations, respectively.

Subgroup analysis per funnel location

A subgroup analysis was conducted to evaluate the impact of funnel location on the angiographical outcomes, specifically assessing the funnel deployment location at the different segments of the ICA: C1, C2/C3, or C4 and above (Figure 3). The primary endpoint was successful reperfusion (eTICI 2b50-3) within 3 ANA passes, with secondary endpoints including eTICI 2c-3 within 3 ANA passes and first pass success for both eTICI 2b50-3 and eTICI 2c-3.

Data regarding the influence of funnel location on angiographical outcome are reported in Figure 3. In general, efficacy was significantly higher when the funnel was deployed beyond the C1 segment of the ICA, in both the ITT and the PP populations.

Successful reperfusion (eTICI 2b50-3) within 3 passes was achieved in the ITT population in 36% of cases with funnel location at cervical C1, which was significantly lower compared to the 89% success rate observed in the petrous C2 and lacerum C3 segments (C2/C3 vs. C1: $p < 0.01$), and to the 71% for C4 and above locations (C1 vs. C4: $p < 0.05$). The rates of successful reperfusion (eTICI 2b50-3) in the PP population were also lower for deployment in C1 (57%), than for deployment in C2/C3 (100%; $p < 0.01$) or C4 and above segments 77% ($p=0.18$). Rates of "Near-complete" reperfusion (eTICI 2c-3) within 3 passes were 36%/57%, 67%/83%, 50%/54% for deployment in C1, C2/C3 and C4 and above segments, in the ITT and PP populations, respectively.

Additional reperfusion outcomes according to funnel deployment location are shown in Figure 3. First pass success rate (eTICI 2b50-3) and "near-complete" first pass rate (eTICI 2c-3) also showed lowest values for C1 compared to C2/C3 and C4 and above segment, being the C2/C3 the highest rates. Raw data are presented in Supplementary Table 4.

Subgroup analysis per aspiration type

A comparative analysis was performed to assess the effectiveness of continuous aspiration (applied from the moment of stent retriever is first pulled back and maintained throughout the entire retrieval process, N=32) versus end aspiration (applied only from the moment in which the stent retriever is introduced inside the funnel, n=11) (Figure 4). Analyses were performed on successful reperfusion (eTICI 2b50-3) within 3 passes and the first pass success rate for eTICI 2b50-3 and eTICI 2c-3.

Results showed that continuous aspiration was significantly more effective than end aspiration in achieving successful reperfusion (eTICI 2b50-3) within 3 passes, with 81%/92% (ITT and PP populations) success in the continuous aspiration group compared to 36%/50% (ITT and PP populations) in the end aspiration group ($p < 0.01$). In terms of achieving complete reperfusion (eTICI 2c-3) within 3 passes, continuous aspiration also led to a higher success rates 63%/75% (ITT and PP populations), compared to 27%/38% (ITT and PP populations) for end aspiration ($p < 0.05$) (Figure 4).

Additional reperfusion outcomes according to aspiration type are shown in Figure 4. The First pass success rate (eTICI 2b50-3) and "near-complete" first pass rate (eTICI 2c-3) also showed highest rates for continuous aspiration compared to end aspiration.

Discussion

In this second in vivo study involving the Anaconda family of funnel devices, the new iteration, which features a substantial simplification of the system, maintained a high rate of complete recanalization. . These findings are consistent with previous in vivo studies on the initial iteration of the device and recent literature data showing a similar safety profile and 90-day disability outcomes[11].

In our study, successful recanalization (eTICI 2b50-3) within 3 passes was achieved in 70% of subjects treated with ANA in the ITT population. In the per-protocol (PP) population, which included subjects adhering strictly to the study protocol, successful recanalization improved to 82%. Importantly, in our study, adherence to specific instructions for the device's use, including the exclusion of subjects presenting with prior intracranial stenosis or stable positioning of the guiding catheter in the higher cervical segments of the internal carotid artery, played a significant role. This is consistent with

observations made when using balloon guide catheters, where positioning in the high cervical segment was associated with improved recanalization[12].

The average median number of passes to achieve eTICI 2b50-3 was 1.0 (IQR 1.0, 2.0) in ITT and 1.0 (IQR 1.0, 2.0) in PP. The number of passes required to achieve successful reperfusion was 1.0 in both the ITT and PP populations. This result is slightly better than what was observed in the initial first-in-man study with the previous iteration of the device (Solonda[9]), where the mean number of passes was 1.6. The First Pass recanalization rate, defined as successful recanalization after a single attempt (eTICI 2b50-3), was observed in 52% and 66% of cases in the ITT and PP populations, respectively. These rates were comparable or even higher superior to recent results reported in other studies[13], suggesting the important role of the funnel in facilitating clot ingestion into the guide catheter.

In our study, we observed a 40.5% rate of any kind of intracranial hemorrhage, which is consistent with findings from previous studies. Specifically, the recently published PROST study reported rates of "any intracranial hemorrhage at 24 hours" as 42.2% with pRESET and 38.9% with Solitaire devices[14] . However, it is important to note that in our study, all cases of intracranial hemorrhage were asymptomatic.

An analysis of the funnel's location impact on angiographic outcomes revealed significantly better recanalization rates when the funnel was positioned within the C2-C3 petrous-lacerum segments of the ICA (intracranial), compared to a lower performance at the C1 cervical segment (extracranial). Interestingly, similar findings have been observed when using other types of balloon guiding catheters in which the efficacy is maximized when positioned more distally in the cervical ICA during thrombectomy[15-20].

Potential reasons might be an increased efficiency in flow restriction when the funnel is deployed in higher and more stable segments of the ICA and a reduced dragging distance of the clot with the stentretriever before ingestion into the funnel, decreasing the possibility of roll-out. The cervical ICA[17], surrounded by the neck's soft tissue, may be prone to collapse during forced aspiration if a BGC or a funnel is positioned too proximal in the C1 segment. In contrast, the petrous ICA is likely more resistant to collapse due to a thick periosteal layer attached to both the vessel and the petrous bone[18]. The collapse of the cervical ICA can reduce suction force and increase the risk of dissection. Additionally, it may cause shearing of the trapped clot during stent retrieval, potentially resulting in distal emboli.

Furthermore, our results demonstrate a distinct benefit of using continuous aspiration, compared to aspiration applied only at the end of the process, in achieving successful recanalization and high first pass success rates. These results are interesting but not surprising. In contrast to end-aspiration, continuous aspiration from the initiation of the retrieval maneuver, combined with the antegrade flow restriction created by the deployed funnel, might create a flow reversal that facilitates the ingestion of the main clot and potential fragments into the funnel. This suggests the advantage of initiating aspiration from the beginning of the stent retrieval procedure.

Limitations

The limitations of the ANAIS study are mainly related to the limited number of patients included. The purpose of the study was however to gather an initial experience of the usability, safety and performance of the device by as many operators as possible. line with this, the single-arm nature of the study is a significant limitation as it does not allow for direct comparison with a control group.

Additionally, the small sample size further limits the ability to draw robust conclusions about the rates of first pass effect and other outcomes. Another limitation, related to the multicenter design, is the involvement of a total of 10 interventionalists treating 42 patients, averaging approximately 4 patients per interventionalist. This reflects the multicentric nature of the study and introduces variability in the procedural techniques and outcomes. It is possible that with increased experience in using the device, both the efficacy results and procedural duration could be improved.However, The promising results helped to confirm the need, and influence the design of a future pivotal trial that will validate its efficacy in safely achieving complete recanalization recanalization in stroke patients.

Conclusions

In this clinical experience, the ANA funnel catheter in combination with a stentretriever achieved a high rate of complete recanalization and a high first pass success, with a good safety profile and favorable 90-day clinical outcomes. The successful reperfusion rate was significantly higher when the funnel was located above the C1 cervical segment of the ICA and when continuous aspiration was applied during the retrieval procedure.

References

1. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke* 2019;50(12):e344-e418. doi: 10.1161/STR.0000000000000211

2. Majoie CB, Cavalcante F, Gralla J, et al. Value of intravenous thrombolysis in endovascular treatment for large-vessel anterior circulation stroke: individual participant data meta-analysis of six randomised trials. *Lancet* 2023;402(10406):965-74. doi: 10.1016/S0140-6736(23)01142-X

3. Jahan R, Saver JL, Schwamm LH, et al. Association Between Time to Treatment With Endovascular Reperfusion Therapy and Outcomes in Patients With Acute Ischemic Stroke Treated in Clinical Practice. *JAMA* 2019;322(3):252-63. doi: 10.1001/jama.2019.8286

4. Garcia-Tornel A, Requena M, Rubiera M, et al. When to Stop. *Stroke* 2019;50(7):1781-88. doi: 10.1161/STROKEAHA.119.025088

5. Tomasello A, Ribo M, Gramegna LL, et al. Procedural approaches and angiographic signs predicting first-pass recanalization in patients treated with mechanical thrombectomy for acute ischaemic stroke. *Interv Neuroradiol* 2019;25(5):491-96. doi: 10.1177/1591019919847623

6. Spiotta AM, Chaudry MI, Hui FK, et al. Evolution of thrombectomy approaches and devices for acute stroke: a technical review. *J Neurointerv Surg* 2015;7(1):2-7. doi: 10.1136/neurintsurg-2013-011022

7. Sanchez S, Cortinas I, Villanova H, et al. ANCD thrombectomy device: in vitro evaluation. *J Neurointerv Surg* 2020;12(1):77-81. doi: 10.1136/neurintsurg-2019-014856

8. Sanchez S, Bailey L, Ducore R, et al. Preclinical evaluation of the ANCD thrombectomy device: safety and efficacy in a swine clot model. *J Neurointerv Surg* 2020;12(10):1008-13. doi: 10.1136/neurintsurg-2019-015548

9. Requena M, Ribo M, Zamarro J, et al. Clinical Results of the Advanced Neurovascular Access Catheter System Combined With a Stent Retriever in Acute Ischemic Stroke (SOLONDA). *Stroke* 2022;53(7):2211-19. doi: 10.1161/STROKEAHA.121.037577

10. Tomasello A, Hernandez D, Pinana C, et al. Mechanical thrombectomy with a novel device: initial clinical experience with the ANA thrombectomy device. *J Neuroradiol* 2022;49(4):324-28. doi: 10.1016/j.neurad.2020.11.003

11. Gupta R, Miralbés S, Calleja Bonilla A, et al. Technique and impact on first pass effect primary results of the ASSIST global registry. J Neurointerv Surg. 2024 Jan 9:jnis-2023-021126. doi: 10.1136/jnis-2023-021126.

12. Moreu M, Gómez-Escalonilla C, Miralbes S, et al. Placing the balloon-guide catheter in the high cervical segment of the internal carotid artery is associated with improved recanalization. J Neurointerv Surg. 2024 Jun 21:jnis-2024-021650. doi: 10.1136/jnis-2024-021650.

13. Lapergue B, Blanc R, Costalat V, et al. ASTER2 Trial Investigators. Effect of Thrombectomy With Combined Contact Aspiration and Stent Retriever vs Stent Retriever Alone on Revascularization in Patients With Acute Ischemic Stroke and Large Vessel Occlusion: The ASTER2 Randomized Clinical Trial. *JAMA* 2021 Sep 28;326(12):1158-1169.

14. Nogueira RG, Lobsien D, Klisch J, et al. Thrombectomy With the pRESET vs Solitaire Stent Retrievers as First-Line Large Vessel Occlusion Stroke Treatment: A Randomized Clinical Trial. JAMA Neurol. 2024 Feb 1;81(2):170-178. doi: 10.1001/jamaneurol.2023.5010.

15. Jeong DE, Kim JW, Kim BM, et al. Impact of Balloon-Guiding Catheter Location on Recanalization in Patients with Acute Stroke Treated by Mechanical Thrombectomy. *AJNR Am J Neuroradiol* 2019;40(5):840-44. doi: 10.3174/ajnr.A6031

16. Milburn J, Vidal G, Gulotta P, et alE-240 Intracranial large bore guide catheter placement is associated with excellent reperfusion: a single institution experience. *Journal of NeuroInterventional Surgery* 2022;14:A210.

17. Klinger-Gratz PP, Schroth G, Gralla J, et al. Protected stent retriever thrombectomy prevents iatrogenic emboli in new vascular territories. *Neuroradiology* 2015;57(10):1045-54. doi: 10.1007/s00234-015-1583-8

18. Sekhar LN, Schramm VL, Jr., Jones NF, et al. Operative exposure and management of the petrous and upper cervical internal carotid artery. *Neurosurgery* 1986;19(6):967-82. doi: 10.1227/00006123-198612000-00012

19. Lee IH, Ha SK, Lim DJ, et al. Distal placement of balloon guide catheter facilitates stent-retriever mechanical thrombectomy for acute ischemic stroke in the anterior circulation. *Acta Neurochir (Wien)* 2023 Dec;165(12):3759-3768.

20. Velasco Gonzalez A, Görlich D, Buerke B, et al. Predictors of Successful First-Pass Thrombectomy with a Balloon Guide Catheter: Results of a Decision Tree Analysis. *Transl Stroke Res* 2020 Oct;11(5):900-909.

Tables

Table 1. Summary of baseline characteristics

Characteristic	ITT (n=43)	PP (n=32)
Age - years	70.5 ± 13.1	71.2 ± 12.7
Female sex	44.2% (19)	50.0% (16)
Pre-stroke mRS:		
mRS 0	65.1% (28)	59.4% (19)
mRS 1	30.2% (13)	37.5% (12)
mRS 2	0% (0)	0% (0)
Hypertension	67.4% (29)	65.6% (21)
Diabetes Mellitus	27.9% (12)	25.0% (8)
Dyslipidemia	39.5% (17)	43.8% (14)
Atrial Fibrillation	41.9% (18)	43.8% (14)
Previous Stroke	9.3% (4)	12.5% (4)
Treated with IV-tPA	37.2% (16)	37.5% (12)
NIHSS score (median, Q1-Q3)	16.0 (13-20)	16.5 (13-20)
ASPECTS (median, Q1-Q3)	10.0 (8.0-10.0)	9.0 (8.0-10.0)
Side of occlusion (left/right)	42.9% (18) / 57.1% (24)	37.5% (12) / 62.5% (20)
Occlusion site:		
TICA	23.3% (10)	18.8% (6)
MCA-M1	53.5% (23)	59.4% (19)
MCA-M2	23.3% (10)	31.3% (10)
Baseline eTICI:		
eTICI 0	95.3% (41)	96.9% (31)
eTICI 1	4.7% (2)	3.1% (1)
Num. interventionalists	10	8
Cases per interventionalist	4.3 ± 3.9	4.0 ± 3.5

((x): number of patients in analysis set, SD: standard deviation, IQR: inter quartile range, NIHSS: National Institute of Health Stroke Scale, ASPECTS: Alberta Stroke Programme Early CT Score, ICA: internal carotid artery, MCA: middle cerebral artery, mRS: modified Rankin Scale).

Table 2. Results of Safety and Efficacy Endpoints assessed by CoreLab and Clinical Event Committee

A) Safety Endpoints	ITT (N=43) proportion (subjects)	Wilson 95% Confidence Interval
Serious Adverse Device Effects (SADE)	0.0% (0)	0.0%, 8.2%
sICHs 24h	0.0% (0)	0.0%, 8.2%
Procedure-related mortality at day 5	0.0% (0)	0.0%, 8.2%
Neurological deterioration 24h[#]	14.6% (6)	6.5%, 28.8%
SADE 5 days*	0.0% (0)	0.0%, 8.2%
All cause-mortality 90 days	14.0% (6)	6.6%, 27.3%
Intracranial hemorrhage 90 days**	40.5% (17)	27.0%, 55.5%
Subarachnoid hemorrhage (SAH)**	16.3% (7)	0.0%, 8.2%
HI-1**	16.3% (7)	0.0%, 8.2%
HI-2**	9.5% (4)	0.0%, 8.2%
Embolization New Territory *post procedural*	0.0% (0)	0.0%, 8.2%
Post Procedural complications	0.0% (0)	0.0%, 8.2%
Vessel Dissection *	0.0% (0)	0.0%, 8.2%
Vessel Perforation *	0.0% (0)	0.0%, 8.2%
Vasospasm	0.0% (0)	0.0%, 8.2%

[#]data available for n=41 subjects
**data available for n=42 subjects

B) Efficacy Endpoints	ITT (N=43)	PP (N=32)
Successful reperfusion (eTICI 2b50-3) ≤ 3 ANA passes	70% [55%,81%]	81% [65%,91%]
First Pass Effect eTICI 2b50-3 (successful reperfusion) (proportion, [95% CI])	51% [37%,65%]	66% [48%,80%]
First Pass Effect eTICI 2c-3 (near complete reperfusion) (proportion, [95% CI])	44% [29%,60%]	56% [38%,74%]
First Pass Effect eTICI 3 (complete reperfusion) (proportion, [95% CI])	33% [19%,47%]	41% [24%,58%]
Near complete reperfusion (eTICI 2c-3) ≤ 3 ANA passes (proportion, [95% CI])	54% [38%,69%]	66% [48%,80%]
Complete reperfusion (eTICI 3) ≤ 3 ANA passes (proportion, [95% CI])	35% [21%,49%]	44% [27%,62%]

B) Efficacy Endpoints	ITT (N=43)	PP (N=32)
Successful reperfusion (eTICI 2b50-3) final (proportion, [95% CI])	95% [89%,101%]	97% [92%,102%]
Number of passes to reach eTICI 2b50-3 (median, Q1-Q3)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
Procedure time (mean ± SD) (minutes)	56.1 ± 38.0	44.3 ± 27.6
Time to treat (mean ± SD) (minutes)	46.8 ± 36.6	35.7 ± 25.7
NIHSS score day 5/discharge (mean ± SD) (median, Q1,Q3)	9.3 ± 10.6 3.0 (1.0-19.0)	8.0 ± 9.6 3.0 (1.0-14.0)
mRS 0-2 (Good Clinical Outcome) (proportion, [95% CI])	52% [38%,67%]	55% [38%,71%]
mRS 0-1 (Excellent Clinical Outcome) (proportion, [95% CI])	38% [25%,53%]	45% [29%,62%]

Figure legends

Figure 1. Schematic drawing and images of thrombectomy using ANA device in combination with a stent retriever. A), B) and C) removal of the clot by the stent retrieval in conjunction with the ANA device, D) image of the stent retriever with the clot inside the funnel outside the patient. (1) Stent retriever deployed stent retriever, (2) ANA expanded funnel, (3) guiding catheter, (4) clot.

Figure 2. Flow chart of the study

Figure 3. Successful reperfusion per funnel location, A) ITT Population B) PP Population

Figure 4. Successful reperfusion per aspiration procedure, A) ITT Population B) PP Population