Mechanical Thrombectomy in Wake-Up Strokes: A Case Series Using Alberta Stroke Program Early CT Score (ASPECTS) for Patient Selection

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Background: There is lack of published studies on mechanical thrombectomy with stent retrievers for wake-up stroke (WUS). *Objective:* To report the outcomes of WUS patients with large vessel occlusions, selected for intervention based on Alberta Stroke Program Early CT Score (ASPECTS) and treated with stent retrievers or primary aspiration thrombectomy. *Methods:* Data were collected retrospectively for each consecutive WUS patient undergoing mechanical thrombectomy with a stent retriever or primary aspiration catheter between February 2015 and September 2016. ASPECTS ≥ 6 was used as the primary imaging criterion for offering thrombectomy in these WUS patients. Main outcomes were the in-hospital improvement in the National Institutes of Health Stroke Scale (NIHSS) and the occurrence of symptomatic hemorrhage. *Results:* Twelve patients were included in this study; 11 were treated with stent retrievers and 1 was treated with primary aspiration thrombectomy alone. Successful recanalization was achieved in 100% of the patients (33% thrombolysis in cerebral infarction [TICI] 2B and 67% TICI 3). Every patient experienced a reduction in the NIHSS during hospitalization, with a mean NIHSS decrease of 11.1 ± 5.1 points. There was a trend for a larger reduction in the NIHSS in patients with TICI 3 compared to TICI 2B recanalization. There was no symptomatic intracranial hemorrhage in our cohort. *Conclusions:* For patients with WUS, careful selection of patients using ASPECTS may allow for safe interventions, with low risk of clinical deterioration, and no-periprocedural mortality. All our patients demonstrated a reduction in their NIHSS after the thrombectomy and clinical improvement. **Key Words:** Acute ischemic stroke—wake-up stroke—mechanical thrombectomy—ASPECTS—stent retrievers.

Introduction

Recent randomized controlled trials (RCTs) have provided Class I evidence for the efficacy of mechanical thrombectomy in acute ischemic stroke patients with large vessel occlusion (LVO) and a witnessed time of onset of their deficits.[1-5] As a result, mechanical thrombectomy with stent retrievers is now considered the gold standard for treating LVO ischemic strokes, irrespective of whether or not intravenous thrombolysis is administered.[6]

Wake-up strokes (WUS), defined as strokes occurring during sleep, account for approximately 10% of acute ischemic strokes.[7] Unfortunately, there are no published RCTs

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of endovascular treatment in WUS patients with LVO. Published studies of endovascular treatment in WUS patients consist mostly of small case series using a combination of intravenous and intra-arterial thrombolysis and/or first-generation thrombectomy devices,[8-10] which are known to result in low recanalization rates, and do not reflect the current clinical practice of using stent retrievers and large bore aspiration catheters for mechanical thrombectomy.[6] To date, there has been only a single published case series reporting the results of stent retriever thrombectomies in WUS patients.[11] Because of the unknown time of onset of symptoms in WUS patients and the lack of RCTs, there is uncertainty regarding the optimal management of this subset of acute ischemic stroke patients. The 2015 American Heart Association/American Stroke Association guidelines for the early management of acute ischemic stroke with endovascular therapy do not discuss the use of mechanical thrombectomy in WUS patients.[6]

The goal of our study was to report the outcomes of WUS patients with LVO, selected for intervention based on their admission ASPECTS (Alberta Stroke Program Early CT Score), and treated with stent retrievers and large bore aspiration catheters.

Materials and Methods

This study was approved by our hospital's Institutional Review Board for retrospective data collection and review. Data were collected retrospectively for each consecutive patient with a "wake-up" stroke undergoing thrombectomy with the Solitaire FR (Covidien, Irvine, CA), or the Trevo (Stryker, Kalamazoo, MI) stent retriever, or primary thrombus aspiration alone with the Penumbra large bore catheters (Penumbra, Alameda, CA). WUS was defined as a stroke occurring during sleep, in patients who were neurologically intact when they went to sleep, but were discovered with symptoms of stroke the following morning. Data from consecutive WUS cases from February 2015 to September 2016 were collected and analyzed.

Our stroke triage protocol consists of noncontrast brain computed tomography (CT), followed by a "one-pass" CT angiogram (CTA) of the brain and whole-brain CT Perfusion (CTP) in a 320 row CT scanner (Aquilion-1, Toshiba, Tustin, CA), as well as a neck CTA. Patients were considered candidates for endovascular therapy if they had a relatively small infarct core on noncontrast CT (ASPECTS ≥ 6), an anterior circulation large vessel occlusion (Internal Carotid Artery [ICA], M1, or M2 segment Middle Cerebral Artery [MCA] occlusion), and National Institutes of Health Stroke Scale (NIHSS) of at least 6. A relatively small infarct core on CT (ASPECTS ≥ 6) was the main criterion for thrombectomy eligibility, whereas a low ASPECTS (<6) was deemed to represent a large infarct core and hence thrombectomy was not offered to these patients. CTP was used as an imaging adjunct to decide on the eligibility for thrombectomy, but the ASPECTS was the main guide on whether or not to offer intervention. Mechanical thrombectomy was performed by 2 physicians (A.A.K. and I.B.R.). Balloon guide catheters with flow reversal and conscious sedation were routinely used in our patients.

The following data were collected from computerized records and imaging studies at the hospital: demographics, admission NIHSS, time of last known well before going to sleep, time of CT/CTA/CTP imaging, time of femoral artery puncture, vessels occluded, time of recanalization, and procedure technical details. Successful recanalization was defined as thrombolysis in cerebral infarction (TICI) score of 2B-3. Magnetic resonance imaging (MRI) obtained 24-36 hours after the intervention was used to assess for hemorrhagic transformation. In patients with contraindications to MRI, a CT was obtained instead. Symptomatic intracranial hemorrhage (sICH) was defined according to the Safe Implementation of Thrombolysis in Stroke-Monitoring Study definition[12]: a type 2 intraparenchymal hemorrhage exceeding 30% of the infarcted volume with significant mass effect, or a subarachnoid hemorrhage leading to a reduction of NIHSS of 4 points or higher, or death. Neurologic outcomes were assessed by a stroke neurologist prior to discharge and were quantified using the NIHSS.

Statistical analysis was performed with a two-tailed *t*-test. For all statistical analyses, $P < .05$ was considered statistically significant.

Results

Baseline Data

A total of 12 patients with WUS were treated with thrombectomy. There were 4 men and 8 women. Mean age was 75.9 years (age range 59-94 years). The mean admission NIHSS was 17.8 ± 6.2. The mean admission ASPECTS was 8.4 (range 6-10). The time from last known normal to CT/CTA/CTP imaging was 12.6 ± 8.0 hrs. The time from last known normal to femoral puncture was 14.0 ± 8.4 hrs, and the time from last known normal to recanalization was 14.7 ± 8.4 hours (Table 1).

Radiological and Clinical Outcomes

Femoral access was used in 10 patients, direct common carotid stick in 1 patient, and brachial access in 1 patient, due to extreme tortuosity of the common carotid origin. There were no cases of failed endovascular access in WUS patients during the study period. Target vessel occlusions were as follows: 3 ICA terminus occlusions, 8 M1, and 1 M2. All 12 patients had successful recanalization, with 4 patients achieving TICI 2B and 8 patients TICI 3 scores. The Solitaire FR stent retriever was used in 10 patients, the Trevo stent retriever in 1 patient, and the Penumbra 5-MAX ACE aspiration catheter in 1 patient who had an unstable calcified fragment from an ICA plaque embolizing the M1 segment of the right MCA.

Table 1. *Demographics, clinical characteristics, and treatment outcomes*

	n (%)
Demographics	
Age (years) (mean ± SD)	75.9 ± 12.6
Female gender (n, %)	8 (67)
Prethrombectomy NIHSS (mean ± SD)	17.8 ± 6.2
Admission ASPECTS (mean ± SD)	8.4 ± 1.3
Occlusion site (n, %)	
ICA terminus	3 (25)
M1 segment of MCA	8 (67)
M2 segment of MCA	1 (8)
Treatment timings	
Time from LKN to imaging (h) (mean ± SD)	12.6 ± 8.0
Time from LKN to femoral puncture (h) (mean ± SD)	14.0 ± 8.4
Time from LKN to recanalization (h) (mean ± SD)	14.7 ± 8.4
Duration of intervention (min) (mean ± SD)	45.1 ± 30.0
Treatment outcomes	
TICI 2B/3 (n, %)	12 (100)
TICI 2B (n, %)	4 (33)
TICI3 (n, %)	8 (67)
Predischarge NIHSS (mean ± SD)	6.7 ± 6.6
Mean NIHSS reduction (mean ± SD)	11.1 ± 5.1
Mean NIHSS reduction in TICI2B recanalization (mean ± SD)	7.3 ± 2.5
Mean NIHSS reduction in TICI3 recanalization (mean ± SD)	13.0 ± 5.1
Patients with >50% decrease in their NIHSS (n, %)	9 of 12 (75)
Higher admission ASPECTS (9, 10) with >50% NIHSS decrease (n, %)	5 of 5 (100)
Lower admission ASPECTS (6, 7, 8) with >50% NIHSS decrease (n, %)	4 of 7 (57)
sICH (n, %)	0 (0)

Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; LKN, last known normal; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage; TICI, thrombolysis in cerebral infarction.

The mean procedure time (femoral puncture to recanalization) was 45.1 ± 30 minutes. Figure 1 is an illustrative example of a 59-year-old female patient with a WUS due to a right M1 occlusion and a right ICA dissection. The admission ASPECTS was 9. A TICI 3 recanalization was achieved and in the follow-up MRI, the patient had only a small lentiform tail infarct, and no cortical infarct or detectable neurological deficits (NIHSS of 0).

The NIHSS had a mean reduction of 11.1 ± 5.1 between the admission (prethrombectomy) NIHSS and the predischarge NIHSS (Fig 2). There was a statistically significant difference between the prethrombectomy NIHSS and the predischarge NIHSS (17.8 ± 6.2 and 6.7 ± 6.6, respectively; $P < .0001$). Patients with TICI 3 recanalization showed a trend for larger reductions in their NIHSS, compared to patients with TICI 2B recanalization, which did not reach statistical significance (13.0 ± 5.1 and 7.3 ± 2.5, respectively; $P = .06$).

Nine patients had a reduction between their admission and predischarge NIHSS of at least 50%, and 3 patients had a reduction of less than 50%. When the patients were divided into higher admission ASPECTS (10 or 9) and lower admission ASPECTS (8, 7, or 6), all 5 of the higher admission ASPECTS patients had an NIHSS decrease of at least 50%, whereas 4 of 7 of the lower admission ASPECTS patients had an NIHSS of at least 50%. Patients with higher admission ASPECTS showed a trend for larger NIHSS reductions, which did not reach statistical significance (5 of 5 and 4 of 7, respectively; $P = .20$).

Adverse Effects

Four patients suffered petechial microbleeds on follow-up MRI studies. There were 3 of 4 petechial microbleeds not readily visible on follow-up CT studies, but only on gradient-echo sequences in the MRI study. One patient had a hemorrhage in the basal ganglia (which were already infarcted), without mass effect. There was no sICH in our cohort. There was no increase in the NIHSS in any of the patients after the thrombectomy procedure, or at any time during hospitalization (Fig 1). There were no periprocedural or in-hospital deaths in the WUS patients treated with thrombectomy.

Discussion

In the present study, we found that when patients with WUS were carefully selected for thrombectomy

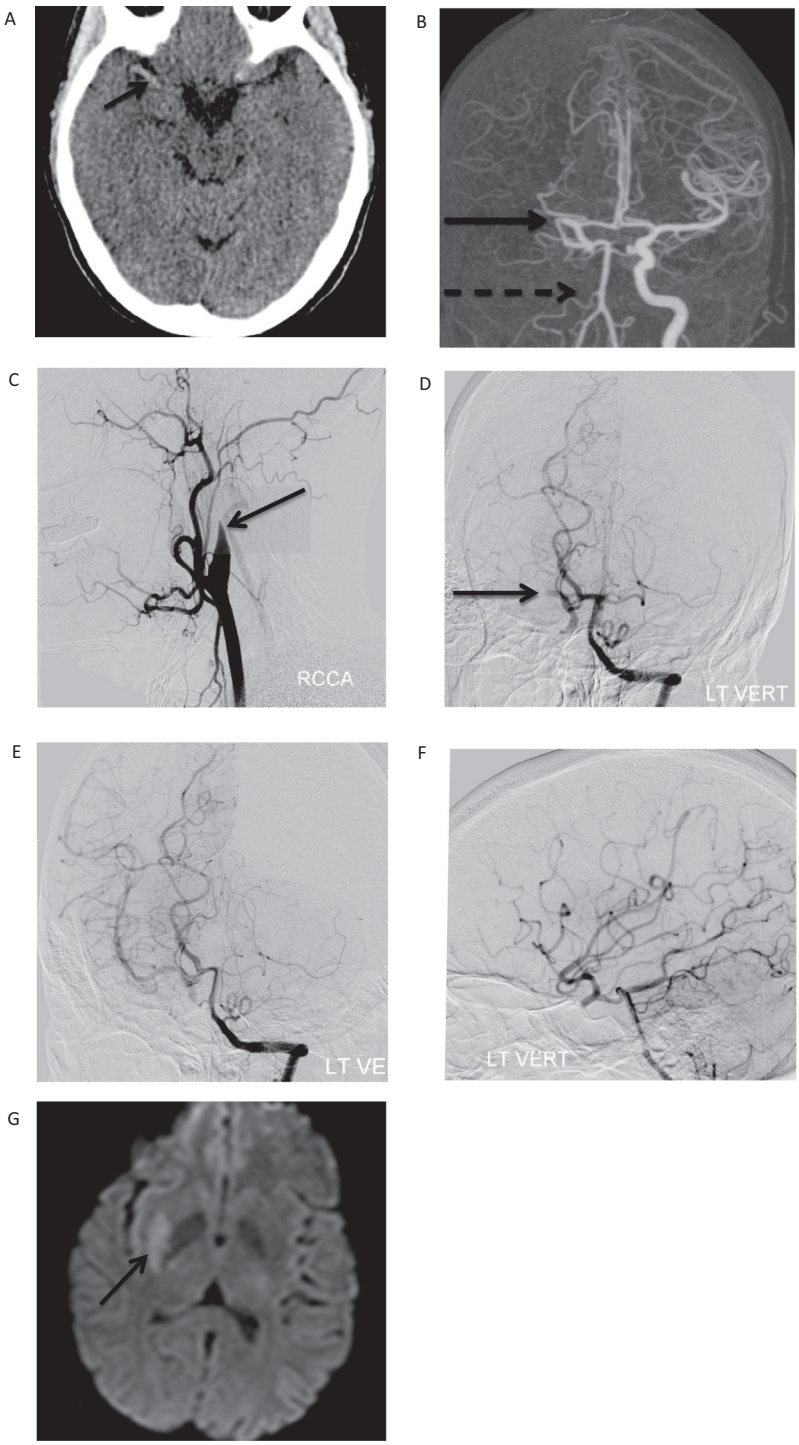

Figure 1. *Illustrative case of a WUS patient. This was a 59-year-old female who presented with left upper extremity weakness, facial droop, and right gaze preference (NIHSS 6). Given that she woke up with these symptoms, no code stroke was activated. (A) A hyperdense right MCA sign (arrow) in the admission CT was seen by the interpreting neuroradiologist. The admission ASPECTS was 9. (B) The CT angiogram demonstrated a proximal right M1 occlusion (arrow) and an occluded right ICA (dashed arrow). The decision was made to proceed with angiography and mechanical thrombectomy, given the large vessel occlusions and the high ASPECTS. (C) Right common carotid angiogram, lateral projection: there is occlusion of the proximal right ICA with a flame-shaped appearance, strongly suggestive of a dissection (arrow). (D) Left vertebral angiogram, AP projection: there is a dominant right posterior communicating artery resulting in retrograde flow to the communicating segment of the right ICA and to the proximal M1, which has an abrupt occlusion (arrow). A microsystem was used to drill through the occluded right ICA and the occluded right M1, with the goal to recanalize the M1 (not shown). Following the deployment of a Solitaire 4 × 20 mm stent retriever and subsequent pull, AP and lateral projection angiograms of the left vertebral artery were performed (E,F): there is recanalization of the previously occluded right M1 with no distal occlusions in the right MCA vascular tree (TICI 3). The large posterior communicating artery supplies sufficient blood to the right MCA territory. Hence, we decided to not attempt a right ICA recanalization, given the risk of distal thromboembolism. (G) Follow-up MRI, DWI sequence: there is a small lentiform tail infarct (arrow shows the restricted diffusion). The rest of the right MCA territory does not show any other areas of restricted diffusion. The patient was discharged home with an NIHSS of 0. Abbreviations: ASPECTS, Alberta Stroke Program Early CT Score; CT, computed tomography; DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; NIHSS, National Institutes of Health Stroke Scale; TICI, thrombolysis in cerebral infarction.*

procedures using ASPECTS, the procedure was safe, without sICH, and no-periprocedural mortality. All our patients demonstrated a reduction in their NIHSS after the thrombectomy, while they were still inpatients. There was a trend for a larger reduction in the NIHSS in patients where TICI 3 recanalization was achieved, compared to patients with TICI 2B recanalization, underscoring the need for high-quality recanalization in LVO patients. Similarly, and not surprisingly, there was a trend for a larger reduction in the NIHSS in patients with higher admission ASPECTS (9 or 10), compared to patients with lower ASPECTS (6, 7, or 8). The vast majority of cases were treated with stent retrievers, balloon guide catheters with flow reversal, and conscious sedation, reflecting the current clinical practice and the American Heart Association/American Stroke Association guidelines for the early management of acute ischemic stroke.[6]

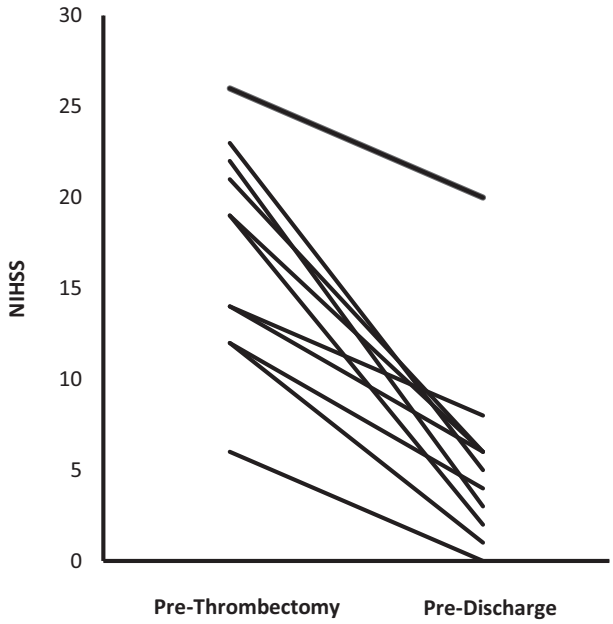

Figure 2. *Prethrombectomy and predischarge (postthrombectomy) NIHSS. Abbreviation: NIHSS, National Institutes of Health Stroke Scale.*

Most of the published studies on endovascular treatment of WUS describe cases treated with first-generation devices, such as the Merci retriever, intra-arterial thrombolysis, or intracranial stenting, techniques that are known to result in lower recanalization rates and are no longer relevant to clinical practice. Moreover, several of the earlier studies group true WUS and strokes with unwitnessed/unknown times of onset together, although these are 2 distinct stroke patient populations.[8,9] Only a recent study by Mokin et al[11] reported outcomes in WUS patients treated with modern stent retrievers and relatively high successful recanalization rates (69% TICI 2B or 3). In our series, all patients had TICI 2B or 3 recanalization rates, likely explaining the symptomatic improvement of all our patients while they were still inpatients. Mokin et al used CTP as the main imaging method to evaluate the extent of salvageable brain tissue versus infarct core, whereas we used ASPECTS to exclude patients with large infarct core.

We used ASPECTS as the primary imaging tool to select patients for thrombectomy, with a cutoff score of 6. Although all our acute stroke patients routinely undergo CTP evaluation in a 320-detector row CT scanner, we decided to use ASPECTS instead of CTP for several reasons. First, there is lack of standardization and validation in acquisition and postprocessing CTP protocols,[13] and there is no consensus regarding the optimal parametric maps to define penumbra and core.[14] Evidence suggests that the distinction between infarct core and penumbra requires the application of threshold values in the cerebral blood volume and cerebral blood flow maps,[15,16] which is not practical in clinical practice. Second, ASPECTS is a reliable, standardized, and reproducible grading system developed to assess early ischemic changes in CT studies,[17] and hence ASPECTS lacks any of the above-mentioned drawbacks of CTP. Finally, ASPECTS was used to select patients eligible for thrombectomy in 3 of the 5 recent RCTs of endovascular treatment for acute stroke (ESCAPE, SWIFT PRIME, and REVASCAT).[3-5] ASPECTS ≥ 6 was the imaging eligibility criterion in the ESCAPE and SWIFT PRIME trials.

There are several limitations to the present study. This is a single-center study, limiting the possibility to generalize the results. The retrospective, observational design is subject to all the limitations inherent with this methodology. Moreover, the postthrombectomy evaluation was limited to the inpatient period. For logistical reasons, such as patient transfers to other facilities due to insurance issues, we were not able to follow-up several patients and we could not report on the 30- or 90-day modified Rankin Scale score.

Our study indicates that endovascular therapy in WUS patients, selected with ASPECTS to exclude large infarct cores, and treated mainly with stent retrievers, is safe and effective. DAWN (Trevo and Medical Management Versus Medical Management Alone in Wake Up and Late Presenting Strokes) and POSITIVE (PerfusiOn Imaging Selection of Ischemic STroke Patients for EndoVascular ThErapy) are ongoing trials designed to include patients with WUS. It is possible that mechanical thrombectomy in carefully selected WUS patients may become the standard of care in the future.

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