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## ABSTRACT

**BACKGROUND:** Observational studies of thrombolysis outcomes in wake-up acute ischemic stroke (AIS) patients selected based on non-contrast brain CT criteria suggested that treated patients did as well as or better than those not treated, after adjustment for baseline characteristics. We began offering thrombolytic treatment (IVTPA) to patients presenting with wake-up strokes and normal non-contrast brain CTs, who could be treated within 4.5 hours of being found.

**DESIGN/METHODS:** A retrospective chart review was performed in patients presenting with AIS between November 2014 and December 2017 who received IVTPA. A planned subgroup analysis compared patients with wake-up strokes and normal non-contrast brain CTs to patients with witnessed stroke treated within 4.5 hours of being found, or of witnessed onset, respectively.

**RESULTS:** Three hundred and six patients were treated, 279 with witnessed and 27 with wake-up strokes. Efficacy and safety were similar in both groups. Discharges home, respectively, were 143(53%) and 13(48%); facility discharges were 112(40.1%) and 11(40.7%) and in-hospital mortality was 19 (6.8%) and 3 (11%). Treatment-related symptomatic bleeds were: 5(1.8%) and 1 (3.7%), respectively.

**CONCLUSIONS:** The findings show that it is safe to treat patients with wake-up strokes and a normal brain CT scan with IV TPA. Demonstrating safe utilization of absence of early ischemic tissue changes on CT to expand thrombolytic treatment eligibility in patients with wake-up stroke suggests that it may be safe to extend beyond 4.5 hours the treatment eligibility window in patients with witnessed stroke onset, when the non-contrast brain CT scan is normal.

## METHODS

The medical records of all patients who received IV TPA for acute ischemic stroke (AIS) at Yitzhak Shamir (Assaf Harofeh) Medical Center (YSMC) between November 2014 and December 2017 (38 months) were reviewed retrospectively. Our primary comparison analyzed outcomes during this period compared to those of the preceding 21 months (February 2013 to October 2014). Patients who received IV TPA and endovascular treatment were first analyzed and reported together with patients who received TPA alone. Post hoc sensitivity analyses examined differences between the two groups. A subgroup analysis of patients treated in the latter period compared patients with wake-up strokes and normal non-contrast brain CT scans who were treated within 4.5 hours of being found to patients with witnessed stroke treated within 4.5 hours of onset. For patients with wake-up strokes and normal CTs – we registered "time found" as "time of onset." We compared, in secondary subgroup analyses, outcomes in patients with more severe strokes, defined by admission NIHSS scores  $\geq 6$  (who would have been included in early thrombolysis series, including our own pre-2013 cohorts) and patients with milder strokes (NIHSS  $< 6$ ). Patient numbers, demographic features, stroke severity, work flow parameters, outcomes, and safety were reviewed. Primary efficacy outcomes were: discharged home, discharged to inpatient rehabilitation or to a nursing home, and death. Safety outcomes were death and symptomatic parenchymal bleeds (PH2).

The study was approved by the YSMC Institutional Review Board (IRB).

## RESULTS

Table 1: Patient Characteristics: Patients with witnessed onset vs. wake-up strokes

	Total	Witnessed onset	Witnessed * onset, TPA only	Wakeup* stroke
Number of patients treated	306	279	254	27
Patients per year	97	88	80	9
Number (%) Men	179 (58.5%)	161 (57.5%)	152 (59.8%)	18 (66.6%)
Age (years) Mean $\pm$ SD	71.3 $\pm$ 13.3	71.2 $\pm$ 13.4	71.1 $\pm$ 13.5	72.0 $\pm$ 13.3
Age range (years)	24-101	24-101	34-101	47-99
Admission NIHSS, Mean $\pm$ SD	8.2 $\pm$ 5.4	8.4 $\pm$ 5.5	7.7 $\pm$ 5.1	6.8 $\pm$ 3.4
NIHSS range	1-32	1-32	1-32	2-17
Patients with NIHSS $\geq$ 6	179(58.5%)	163 (58.4%)	138 (54%)	16 (59.3%)
Time, onset to ER (min) ---- Range	87 $\pm$ 46 0-213	87 $\pm$ 47 0-213	88 $\pm$ 46 0-213	87 $\pm$ 43# 30-178
Time, ER to treatment (min) ----Range	82 $\pm$ 35 26-201	81 $\pm$ 34 26-201	83 $\pm$ 34 26-201	87 $\pm$ 36 49-177
Time, onset to treatment (min) ---- Range	169 $\pm$ 54 59-330	168 $\pm$ 54 59-330	172 $\pm$ 52 60-330	174 $\pm$ 54# 90-270

#Wake-up time to ER or to treatment

\*Differences between witnessed and wake-up strokes, TPA only treatment: p=NS

Table 2 : Patient Outcomes: Patients with witnessed onset vs. wake-up strokes

	Total	Witnessed onset	Witnessed onset* TPA only	Wakeup* stroke TPA only (all)
Number of patients treated with IV TPA	306	279	254	27
Number TPA+EV	25 (8.1%)	25	0	0
<b>DISPOSITION – ALL</b>				
Discharged Home	161 (52.6%)	148 (53.1%)	142 (56%)	13 (48.1%)
Discharged to Rehab / NH	123 (40.2%)	112 (40.1%)	95 (37.4%)	11 (40.7%)
Deceased	22 (7.2%)	19(6.8%)	17 (6.7%)	3 (11.0%)
Transferred	20 (6.5%)**	19 (6.8%)	8 (3.2%)	1 (3.7%)
Transfers, annual	6.3			
<b>INTRACRANIAL BLEEDS</b>				
Total (PH1 & PH2)*	15 (4.9%)	14 (5%)	10 (3.3%)	1 (3.7%)
Symptomatic	6 (2%)	5 (1.8%)	4 (1.3%)	1 (3.7%)
---% of NIHSS $\geq$ 6	5/179=2.8%	4	3	1
---% of NIHSS $<$ 6	1/127= 0.8%	1	1	0
<b>DISPOSITION BY ADMISSION NIHSS</b>				
NIHSS $\geq$ 6 (N)	179 (58.5%)	163 (58.4%)	138 (54%)	16 (59.3%)
Discharged Home	70 (39.1%)	63 (38.6%)	57 (41.3%)	7 (43.7%)
Discharged to Rehab/NH	90 (50.2%)	83 (50.9%)	66 (47.8%)	7 (43.7%)
Deceased	19 (10.6%)	17 (10.4%)	15 (10.8%)	2 (12.5%)
NIHSS $<$ 6 (N)	127	116	116	11
Discharged Home	91 (71.6%)	85 (73.2%)	85 (73.2%)	6 (54.5%)
Discharged to Rehab/NH	33 (26.0%)	29 (25.0%)	29 (25.0%)	4 (36.3%)
Deceased	3 (2.3%)	2 (1.7%)	2 (1.7%)	1 (9.0%)

\*All differences are not statistically significant

\*\* 11 Received endovascular treatment

## CONCLUSIONS

1. It is safe to treat patients with wake-up strokes and a normal brain CT scan with IV TPA.
2. It may be safe to extend beyond 4.5 hours the treatment eligibility window in patients with witnessed stroke onset, when the non-contrast brain CT scan is normal.