



# Safety of Thrombolytics in Patients with Malignancy and Acute Ischemic Stroke

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## INTRODUCTION

Approximately 15% of the patients with malignancy have cerebrovascular disease<sup>1</sup>. These patients are at significant risk for ischemic stroke<sup>2</sup> due to co-morbid vascular disease<sup>3</sup> and hypercoagulability<sup>4</sup>. In rare instances, cerebrovascular disease may be the presenting sign of malignancy<sup>5</sup>. IV t-PA is the only treatment for acute stroke within 3 hours of symptom onset. Little is known about the risk of thrombolytic therapy in patients with malignancy, as these patients have generally been excluded from most clinical trials. This lack of safety data may contribute to concerns about use of t-PA in patients with malignancy in routine practice, or to delays in drug delivery. We sought to evaluate the safety of thrombolytic therapy in patients with acute ischemic stroke (AIS) and malignancy.

## METHODS

Consecutive AIS patients admitted from 1/03 to 12/06 (n=2148) were analyzed retrospectively to identify those treated with thrombolysis. A trained physician abstracted data according to the Get With The Guidelines-Stroke coding instructions. Malignancy was identified based on past history or work-up during the index AIS admission. Malignancy was defined as Past History of Malignancy Only (PHMO) for patients who were without evidence of metastatic disease, who had completed any planned treatments and who were described as having history of malignancy only. Patients with metastatic disease, those undergoing current treatment for malignancy or those who were offered treatment but refused, were classified as having Current Malignancy (CM). Any bleeding during the first 36 hrs after tPA was recorded, and symptomatic bleeding was defined as follows:  
Serious systemic bleeding as a decrease in Hct>15% requiring transfusion of >3 units PRBC; Symptomatic ICH as hemorrhage on brain imaging and clinical worsening attributed to the bleeding. PT/INR, Platelet, anti-thrombotic use, D-dimer, DVT/PE and any previous history of bleeding/clotting were recorded. Univariate analyses were by chi-square. Logistic regression with backward elimination was used to identify independent predictors of in-hospital mortality.

## RESULTS

- 308 of 2148 (14.3%) cases of AIS were treated with thrombolytic therapy
- 210/308 (68%) received IV tPA without IA therapy (IAT), 41 (13%) IV tPA + IAT, and 57 (18%) IAT only
- 44 of 308 (14%) patients who received thrombolytic therapy had malignancy
  - breast, 21%; lung, 18%; colon, 16%; hematologic, 9%; prostate, 9%; skin, 9%; others, 18%
- Metastasis was documented in 11/44 (25%) patients
- Current malignancy (CM) was present in 18 of 44 (34%); 7 of those patients died in-hospital
- Patients with end-stage malignancy receiving palliative care are generally not treated with thrombolytics at our institution, and there were no patients in the study period who received thrombolytics in this setting
- Overall Symptomatic intracranial hemorrhage (SX ICH) was 3.3%
- There were no minor bleeding events in malignancy

Table 1. Patient Characteristics

Patient Characteristic	Malignancy (N=44); %	No Malignancy (N=264); %	P value
Age (mean ± SD)	75.1 ± 10.4	69.6 ± 14.9	0.02
Gender (female)	52.2	50.8	0.85
NIHSS initial (mean ± SD)	15.8 ± 7.4	14.6 ± 6.8	0.49
CAD/MI	36.4	23.5	0.07
Diabetes	14.3	18.9	0.2
Hypertension	70.5	65.5	0.52
Atrial Fibrillation	29.6	26.5	0.67
Dyslipidemia	18.1	15.9	0.71
Prior Stroke/TIA	18.2	14.4	0.51
Smoking	36.4	31.8	0.55
Warfarin Use	9.1	5.3	0.32
PT > 15	15.9	14.5	0.80
Platelet count (mm <sup>3</sup> )	241,300	253,000	0.001
tPA, IV only	72.7	67.4	0.48
Serious systemic hemorrhage	2.3	2.3	1.0
Symptomatic ICH	6.8	2.7	0.14
Any ICH on imaging	29.5	28.8	1.0
Ambulatory at discharge	47.7	62.1	0.07
Mortality	36.4	19.7	0.01

Table 2. Multivariate Model of In-hospital Mortality

Characteristic	Adjusted OR	95%CI	P value
Age	1.01	0.98-1.03	0.64
NIHSS	1.20	1.13-1.27	<0.001
HTN	2.79	1.20-6.28	0.01
Smoking	0.39	0.19-0.82	0.01
Malignancy	2.52	1.09-5.82	0.03

- A documented history of hypertension and malignancy were significantly and independently associated with increased in-hospital mortality, and current smoking (any cigarettes in the past year) with a decrease in in-hospital mortality
- Worsening medical conditions (pulmonary edema, sepsis, advanced pancreatic cancer, bronchitis etc) contributed substantially to in-hospital mortality among the 44 malignancy + thrombolytic patients, more often among those with CM vs. PHMO (71.4% vs. 11.1%; p=0.03). CM was similar to no malignancy and PHMO group in stroke severity (mean NIHSS 17 vs. 14, p=0.8)

## DISCUSSION

- Malignancy was independently associated with increased in-hospital mortality following thrombolysis for AIS at our institution
- Although SX ICH after thrombolytics was higher in malignancy than in no malignancy (6.8% vs. 2.7%), it was not significant and comparable to rate of 5.9% reported in studies
- The mortality in the malignancy does not appear to be due to increased rates of SX ICH or hypercoagulability, but rather due to co-morbid medical conditions. The presence of other major medical problems may have led to the decision to withdraw care in the face of a poor neurologic prognosis
- Without an appropriate control group, we cannot exclude a beneficial effect of thrombolysis in this group despite the higher mortality
- These data suggest that IV and IA thrombolysis can be given without excess risk of bleeding to patients with malignancy. The decision to treat should take into account the degree of medical disability and likelihood of continued care if there is no neurologic improvement

## REFERENCES

1. Arboix A. Cerebrovascular disease in the cancer patient. Rev Neurology. 2000 Dec 16-31;31(12):1250-2.
2. Navi BB, Deangelis LM, Segal AZ. Multifocal strokes as the presentation of occult lung cancer. J Neuro-oncol 2007 Dec;85(3):307-9.
3. Li SH, Chen WH, Tang Y, Rau KM, Chen YY, Huang TL, Liu JS, Huang CH. Incidence of ischemic stroke post-chemotherapy: a retrospective review of 10,963 patients. Clinical Neurology and Neurosurgery. 2006 Feb;108(2):150-6.
4. D. M. Cestari, MD, D. M. Weine, MD, K. S. Panageas, DrPH, A. Z. Segal, MD and L. M. DeAngelis, MD. Stroke in patients with cancer: incidence and etiology. NEUROLOGY 2004;62:2025-2030.
5. Rogers LR. Cerebrovascular complications in cancer patients. Oncology 1994 Jun;8(6):23-30.