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# Short Term Outcome and Associated Factors among Stroke Patients Given Thrombolysis

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Abstract: The study aimed to investigate the short-term outcome and associated factors among acute ischemic stroke patients given rTPA (Recombinant tissue plasminogen activator). This is a hospital-based cross-sectional retrospective study among 107 acute stroke patients given rTPA for a span of 3 years. A favorable outcome is defined as the modified Rankin Scale (MRS) 0 to 2, while a score > 2 is defined as a poor outcome. Mortality and adverse events were also documented. The majority (57%) had favorable outcomes on discharge. Initial stroke severity, stroke etiology, and presence of symptomatic Intracerebral hemorrhage (ICH) were significant factors for discharge outcome. There was no significance as to age group and as to needle time of 0-3 hours versus 3-4.5 hours. The symptomatic ICH rate is 5.6%. The overall mortality rate is 15.88% (47% due to malignant infarction, 17.6% due to symptomatic intracerebral hemorrhage (sICH), 23.52% due to basilar artery occlusion (BAO), and 11.7% due to medical causes). With a dose of 0.6mg/kg, our data indicate favorable discharge outcomes of thrombolysis. A high baseline NIHSS, cardioembolic stroke etiology, and the presence of sICH are seen in patients with poor outcomes. The rate of sICH is consistent with other literature, however with high mortality (100%). Overall mortality is high primarily due to malignant infarct. Institutions must be capacitated to address outcomes and complications of thrombolysis.

Keywords: thrombolysis, outcome, Philippines, patients, Stroke

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## INTRODUCTION

More than 20 years have passed since the birth of thrombolysis. Subsequent research was done in different countries and different nationalities – all geared towards reducing long-term disability with the least complications. With increasing life expectancy and lifestyle changes, the burden of stroke is rising. The majority of stroke burden is in developing countries, comprising 75.2% of deaths and 81% of DALYs (Suwanwela & Poungvarin, 2016). In the Philippines, stroke is the second leading cause of death (after cardiac disease) with a prevalence rate of 0.9%, and ranks fifth among specific diseases with the greatest burden (Navarro et al., 2014).

Emergency management of AIS is focused on attaining vascular reperfusion as soon as possible, without risking the patient's safety, most commonly with intravenous tissue plasminogen activator (tPA) (Lees et al., 2016). The benchmark study organized by the National Institute of Neurological and Communicative Disorders and Stroke (NINDS) provided evidence of benefit later from intravenous rtPA given within 3 hours, led to improved clinical outcome at 3 months at the expense of a 6% risk of symptomatic intracerebral hemorrhage (sICH) ("Tissue Plasminogen Activator for Acute Ischemic Stroke.," 1995). In the ECASS III trial, a benefit was seen for tPA administration within the 3 to 4.5 hour range, however with some exclusions (Hacke et al., 2008). In the International Stroke Trial (IST3), benefits did not diminish among patients more than 80 years old who underwent thrombolysis (Sandercock et al., 2012). Due to sICH, the Japan Alteplase Clinical Trial or J-ACT administered rTPA

at a lower dose of 0.6mg/kg to Japanese patients and resulted in clinical efficacy and safety that are compatible with data reported in North America and European Union for 0.9mg/kg dose (Yamaguchi et al., 2006). In 2016, the Enhanced Control of Hypertension and Thrombolysis in Stroke Disease (ENCHANTED) trial, an open-labeled clinical trial involving predominantly Asian patients with acute ischemic stroke within 4.5 hours, did not show the non-inferiority of low-dose alteplase (0.6mg/kg) to standard-dose alteplase (0.9mg/kg) concerning death and disability at 90 days. However, there were significantly fewer symptomatic intracerebral hemorrhages with low-dose alteplase (Anderson et al., 2016). Although outcome at 3 months had been the standard timeline, a few studies on short-term outcomes show that stroke patients given rTPA are more likely to be discharged directly home after hospitalization. The favorable outcome *modified Rankin Scale (MRS)* (MRS 2 and below) at the time of hospital discharge is significantly associated with lower NIHSS values at admission (Ifejika-Jones et al., 2011).

Intravenous rTPA is an approved cure for acute stroke with favorable short- and long-term outcomes. Although approved in the country in 1999, it was in 2016 when rTPA was available in the institution, and since then, is readily administered to eligible candidates. However, the outcomes of thrombolysis among the Filipino population remain to be seen and have been approached cautiously. A retrospective study done in the Philippines revealed good outcomes of MRS 0 to 2 on discharge (51.1%) and at 3 months (73.1%). However, in-hospital mortality was high at 14.6% (Navarro et al., 2018). Our study aims to determine the short-term outcomes and complications of acute ischemic stroke patients given rTPA in our institution. Furthermore, it aims to determine the association of MRS on discharge and the following: age, stroke etiology, stroke severity, and adverse events (hemorrhagic conversion, extracranial bleeding, orolingual edema).

#### **METHODS**

The study is a retrospective observational cross-sectional study of acute ischemic stroke patients given rTPA in a government tertiary center, from January 2016 to January 2019. Inclusion criteria: (1) > 18 years old (2) clinical diagnosis of ischemic stroke (3) computed tomography (CT) or magnetic resonance imaging (MRI) indicating no intracranial hemorrhage. Exclusion criteria: (1) final diagnosis is a stroke mimicker (2) documented outcome parameter is incomplete (3) transfer to another institution (4) MRS 3 and above for post stroke patients. This study utilized total enumeration, involving the entire population of all stroke patients, resulting in a sample size of 1939.

Charts and medical records of enrolled patients were reviewed. The demographic profile, baseline NIHSS score, vascular territory, stroke etiology by TOAST classification, risk factors, rTPA dose, and needle time were documented. RTPA was given at a dose ranging from 0.6mg/kg to 0.9mg/kg. Weight was estimated. The patients received standard stroke care secondary prevention and in-hospital rehabilitation following current recommendations. A repeat head CT scan was done 24 hours after thrombolysis, or earlier when there was neurologic deterioration. Hemorrhagic transformation was documented. The mortality rate and other adverse events such as bleeding elsewhere in the body, and orolingual edema were documented. Functional outcome on discharge was dichotomized into 2 groups as follows: Good outcome was defined as MRS score of 0 to 2, while poor outcome was defined as MRS 3 to 6.

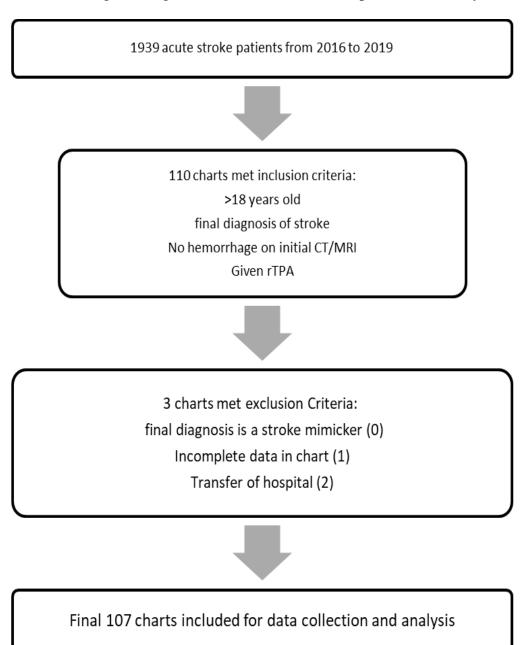
No monetary benefits were given to participants of the study. There is no conflict of interest in the use of rTPA. Confidentiality of data and anonymity of patients were ensured. All the data gathered were kept confidential using pseudonyms/codes. The study commenced upon Ethical Review Committee approval. The study was approved by the ethics committee of the institution.

Descriptive statistics for baseline and demographic data are presented. The association of MRS and the age group, baseline NIHSS, stroke etiology, and adverse events are analyzed using the statistical package of social sciences. ANOVA was used as analytical statistics; the alpha level is set at 0.05.

#### **RESULTS**

Out of 1939 acute ischemic stroke patients admitted, 110 were potentially eligible. **Inclusion criteria are as follows:** (1) age > 18 years old (2) clinical diagnosis of ischemic stroke (3) CT or MRI indicating no hemorrhage. Total enumeration was done. Medical records of patients were reviewed. Three (3) were excluded due to the transfer of hospital (2) and incomplete data in the chart (1), finally arriving at a study population of 107 (<u>Figure 1</u>).

Figure 1. Figure 1 shows the data collection process in the study



<u>Table 1</u> shows demographics, baseline characteristics, and risk factors for stroke. There were more males (63.55%) and the majority were within 45 to 79 years. The mean age was 58 years, ranging from 20 to 88. 17.75% were stroke in the young and 6.54% were more than 80 years old.

Table 1. Clinico Demographic Profile of enrolled patients (n=107)

Age (mean age = 58)	Frequency	Percentage %
18-45 (stroke in the young)	19	17.75
46-79	81	75.70
80 & above	7	6.54
Sex		
Male	68	63.55
Female	39	36.44
Intake within the past 24 to 48 hours of the antip	platelet and anticoagulant	
Aspirin	4	3.73
Clopidogrel	2	1.87
Rivaroxaban	2	1.87
Risk Factors		
HTN	88	82.24
CAD CHF	23	21.50
AF	18	16.88
DM	17	15.88
Previous stroke	11	10.28
Dyslipidemia	8	7.48
Smoker	8	7.48
Alcoholic	5	4.67
Stroke etiology		
Large Artery Atherosclerosis	53	49.50
Cardioembolic	45	42.05
Small vessel occlusion	4	3.73
Cryptogenic	5	4.67
Score severity		
NIHSS score 0-5 (mild)	23	21.5
NIHSS score 6-21 (moderate)	73	68.22
NIHSS score >22 (severe)	11	10.28
Median NIHSS	11	
Mean baseline NIHSS (range 1 to 26)	12	
Vascular territory		
Anterior Circulation	93	86.92
RMCA	54	50.47
LMCA	30	28.03
RICA	5	4.67
LICA	2	1.87
RACA	2	1.87
Posterior Circulation	14	13.08
Basilar Artery occlusion	8	7.48
Pons	2	1.87
LPCA	1	0.93
RPCA	1	0.93
Medulla	1	0.93
Cerebellum	1	0.93
Dose		
0.6mg/kg	95	88.79
0.9mg/kg	12	11.21

Initial Blood Pressure		
Systolic BP	165 (90 to 260)	
Diastolic BP	97 (60 to 150)	
Needle time		
0-3 hours post ictus	73	68.22
More than 3 hours	28	26.17
Wake up stroke	1	0.93
Onset to door time (average)	74 minutes	
Door to Scan time (average)	33 minutes	
Scan time less than 20 minutes	39	36.45
Door to Needle time (average)	94 minutes	
Door to needle time less than 60 minutes	26	24.30
Average onset to needle time	149 minutes	
In-hospital stroke	9	8.41
Admitting diagnoses of in-hospital strokes		
CKD	2	2
Community Acquired Pneumonia	4	4
COPD	2	2
Transient ischemic attack	1	1
L. Baseline Imaging		
CT scan	106	99
MRI stroke protocol	1	1
M. Neurosurgical Procedure		
1. Hemicraniectomy	4	4
2. Tube ventriculostomy	1	1
N. Hospital Days	8.69 (1 TO 42)	

Four patients took Aspirin, 2 patients took Clopidogrel and 2 other patients took RIvaroxaban prior to thrombolysis. The mean systolic BP and diastolic BP was 165/97. Hypertension (82.24%) was the prevalent risk factor, followed by cardiac disease namely CHF and AF (38.31%) then diabetes mellitus (15.88%). The majority of patients (68.22%) had moderate strokes of thrombotic etiology at the MCA territory. Around 13% were infarcts of the posterior circulation. Nine cases (8.41%) were in-hospital strokes and interdepartmental referrals. One of them was managed by the department of neurology as a case of Transient Ischemic Attack who had a stroke while admitted. The other 8 in-hospital strokes were managed by the Department of Internal Medicine primarily due to pulmonary disease (6 cases) and Chronic Kidney Disease (2 cases).

Most of the patients (88.79%) received a dose of 0.6mg/kg of rTPA. The average onset of stroke to door time was 74 minutes. The average door to scan time was 33 minutes. Average door to needle time was 94 minutes and average needle time was 149 minutes. The mean length of hospitalization was 9 days with a range of 2 to 42 days.

A favorable outcome on discharge defined as MRS 0 to 2 was achieved by 57%. Of those who had good outcome, half of them had a discharge MRS score of 1. Poor outcome was seen in 42.99% and the majority of them were MRS 3 on discharge. The hemorrhagic conversion was seen in 14.01%, and the majority were asymptomatic. Six patients (5.60%) had symptomatic ICH, of whom all of them died. 4.67% had bleeding outside the CNS which was uncomplicated. 15.88% had malignant infarct of whom half had died due to brain herniation. Eight patients (7.48%) had Basilar Artery Occlusion and 4 of them died (Table 2).

Table 2. Outcome of thrombolysis: MRS, Adverse Events, Death

Outcome of Thro	mbolysis	Frequency	Percentage %	
Functional outcome on Discharge				
Good outcome Ml	RS 0 to 2	61	57	
Poor outcome MR	S 3 to 6	46	42.99	
MRS 0		20	18.69	
MRS 1		31	28.9	
MRS 2		10	9.34	
MRS 3		20	18.69	
MRS 4		5	4.67	
MRS 5		4	3.74	
MRS 6		17	15.88	
Hemorrhagic Con	version	15	14.01	
Asympto	matic ICH	9	60	
Sympton	natic ICH	6	40	
Bleeding outside (	CNS	5	4.67	
Gum		3	60	
GI		2	40	
Deaths		17	15.88	
1. Neurolo	gic	15	14	
Malignar	nt Infarct	8	7.47	
sICH		6	5.6	
Basilar A	rtery Occlusion	4	3.7	
2. Medical		2	1.9	

Overall Mortality rate during the hospital stay was 15.88% (n=17). In 15 patients, the cause of death was neurologic while 2 deaths were due to medical causes namely fatal arrhythmia and acute respiratory failure. The study investigated the relationship between age group, needle time, stroke severity, stroke etiology, presence of hemorrhagic conversion, and discharge outcome (see <u>Table 3</u>). There was no significance as to age group and needle time. Stroke etiology is a significant factor in discharge outcome revealing cardioembolism as a factor for poor discharge outcome. Severe stroke and sICH are associated factors for poor discharge outcomes.

None of the patients with a needle time of more than 4.5 hours had symptomatic hemorrhage. The average needle time was 327 minutes. Baseline NIHSS ranged from 5 to 26, with a mean NIHSS of 16. Among those with hemorrhagic conversion (see <u>Table 4</u>), most of the patients were males with a mean age of 60 who received rTPA at 0.6mg/kg dose. The mean NIHSS was 15 and the majority had cardioembolic strokes (80%) of the MCA territory. Around 60% had hemorrhagic transformation (HT) while 33% had parenchymal hematoma (PH). Overall, the majority had poor outcomes (60%).

In the subgroup analysis of the mortality cases in the study (see <u>Table 5</u>), the mean age was 60 and most of them were males (64.7%). The majority (64.7%) had a moderate stroke and 29.4% had a severe stroke, with a mean baseline NIHSS of 15. Most (70.59%) had cardioembolic strokes of the right MCA territory (5.9% LMCA territory), 23.5% had basilar artery occlusion, and 18% patients had ICA occlusion. The mean baseline blood pressure was 180/100mmHg. Four patients had comorbidities namely CAP HR, CKD, COPD, and RHD in CHF. The average needle time was 165 minutes, of whom, the majority (16/17) received a dose of 0.6mg/kg. Thrombectomy is not available in the institution. A few patients were able to avail of surgical intervention due to financial difficulties. Of the fifteen (15) mortality cases who had neurologic causes of death, three patients underwent decompressive hemicraniectomy and one underwent tube ventriculostomy.

Table 3. The association of MRS on discharge and age, stroke severity, stroke etiology, hemorrhagic transformation and other adverse events

	X7 1. 1 -		hemorrhagic transformation and other adverse events				
	Variable	<del> </del>	MRS Upon Discharge		P-Value		
		Good	Poor	10			
	18-45	14	4	18			
Age	46-79	42	40	82			
	80 above	5	2	7	0.226 <sup>ns</sup>		
Total		61	46	107			
Mean Ran	ık	51.67	57.09				
	Thrombotic	37	15	52			
Etiology	Cardioembolic	16	30	46			
Ellology	Cryptogenic	4	1	5			
	Small vessel	4	0	4	0.050*		
Total		61	46	107			
Mean Ran	ık	49.42	60.08				
	Mild	23	1	24			
Severity	Moderate	37	35	72			
	Severe	1	10	11	0.000**		
Total		61	46	107			
Mean Ran	ık	43.08	68.48				
Needle	0-3 hours	41	32	73			
Time	3 to 4.5 hours	19	11	30	1		
Time	>4.5 hours	1	3	4	0.797 <sup>ns</sup>		
Total		61	46	107			
Mean Ran	ık	54.54	53.28				
	None	56	33	89			
Adverse	sICH	0	6	6			
Event	asICH	3	6	9			
	extra cranial	2	3		0.011*		
Total		61	46	107			
Mean Ran	ık	49.70	59.70				

<sup>\*-</sup> significant at .05 \*\*- highly significant at 0.01 ns-not significant

Table 4. Clinico Demographic profile of 15 thrombolysis patients who had Hemorrhagic Conversion

Hemorrhagic Conversion					
Patient's Characteristics	Frequency	Percentage %			
Mean Age	60 (range: 39 to 76)				
Sex	10 males	66.67			
Intake of antiplatelet within 24 hours	1 (Clopidogrel)	6.67			
rTPA dose 0.6mg/kg	15	100			
Mean Blood Pressure	179/107				
Deranged platelet count	0	0			
Deranged PT	0	0			
Deranged aPTT	0	0			
Stroke Severity: Mean NIH	SS 15 (NIHSS range: 5 to 25)				
Mild	1	6.67			
Moderate	11	73.33			
Severe	3	20			
Vascular	Territory				
Right MCA	8	53.33			
Left MCA	3	20			
Right ICA	3	20			
Stroke	Etiology				
Cardioembolic	12	80			
Thrombotic	3	20			
Type of Hemorr	hagic Conversion				
1. Hemorrhagic transformation	9	60			
2. Parenchymal Hematoma	5	33.33			
3. Remote parenchymal hematoma	1	6.67			
Extracranial bleeding	2	13.33			
Discharge outcome					
MRS 0	0	0			
MRS 1	0	0			
MRS 2	3	20			
MRS 3	2	13.33			
MRS 4	1	6.67			
MRS 5	1	6.67			
MRS 6/ Death	8	53.33			
Good outcome MRS 0 to 2	3	20			
Poor outcome MRS 3 to 6	12	80			

Table 5. Clinico Demographic profile of thrombolysis patients who died during hospital stay

Patient's Characteristics (n=17)	Frequency	Percentage %
Mean Age	60 (age range: 43 to 82)	
Sex	11 males	64.7
Intake of antiplatelet within 24 hours	1 (Clopidogrel)	5.88
Mean Blood Pressure	179/107	
rTPA dose 0.6mg/kg	16	94.12
0.9mg/kg	1	5.88
Average onset to needle time	165 minutes	
Risk Factors		
Hypertension	15	88.24
Diabetes	3	17.65
Atrial Fibrillation	6	56.07
CAD/CHF	5	29.41
s/p CVD	2	11.76
Smoker	2	11.76
Alcoholism	1	5.88
Stroke Severity	Median NIHSS 15	
Shoke Severity	(range: 5 to 25)	%
Mild	1	5.8
Moderate	11	64.7
Severe	5	29.4
Vascular Territory		
Right MCA	9	52.9
Left MCA	1	5.9
Right ICA	2	11.76
Left ICA	1	5.9
Basilar Artery	4	23.5
Stroke Etiology	<u>-</u>	20.0
Cardioembolic	12	70.59
Thrombotic	5	29.4
Cause of Death		27.1
Neurologic	15	88.23
Medical	2	11.76
Comorbidities	2	11.70
	1	E 00
CAP HR	1	5.88
Chronic Kidney Disease RHD in CHF	1	5.88 5.88
COPD in exacerbation	1 1	5.88
	1	5.88
Hemorrhagic Conversion	2	14 77
Asymptomatic	2	11.76
Symptomatic	6	3.53
Procedures	2	15.45
Hemicraniectomy	3	17.65
Tube ventriculostomy	1	5.88
In hospital stroke	2	11.76
Average hospital stay	5.6 days	

# **DISCUSSION**

In general, the results show that acute ischemic stroke patients given rTPA benefit from thrombolysis upon hospital discharge (57%).

#### Age

The mean age of patients in our study was 58 years, which is 9 years lower than the mean age of patients in the NINDS trial (67). Our study showed no significant difference in outcome among the

different age groups receiving alteplase. Of the 7 patients aged >80 given rTPA, 5 of them had good outcome on discharge. As stated in the **IST-3** study, benefit was suggested in the primary outcome among those aged 80 and above (Sandercock et al., 2012). Regarding sICH, a meta-analysis including studies comparing the risk of sICH in patients receiving alteplase who were >80 and <80 years of age demonstrated no statistically significant difference in risk between groups (Demaerschalk et al., 2016). On the other end, young adults with ischemic stroke given intravenous thrombolysis also have favourable outcomes as in other studies (Putaala et al., 2009; Toni et al., 2012).

Consistent with studies, the results showed that initial stroke severity is a strong significant factor of discharge outcome. Majority of our patients had moderate stroke (68.22%). Of the 24 patients with mild stroke, only 1 had poor outcome. Ten (10) out of 11 patients with severe stroke had poor outcome. Despite severity, there should be no upper limit of NIHSS score for patients otherwise eligible for alteplase presenting to medical attention. Although the chances of a good outcome were less overall, severe stroke patients still had a better chance of a good outcome with alteplase treatment than without treatment. In fact, severe stroke has been associated with increased risk of sICH with or without thrombolysis (Demaerschalk et al., 2016).

#### Needle time

Stroke severity

The average onset to door time is 74 minutes, door to needle time is 94 minutes and the average onset to needle time is 149 minutes. Standard protocol requires a door to needle time less than 60 minutes, and scan time less than 20 minutes in at least 50% of patients managed. In our institution, 24.30% achieved a door to needle time of less than 60 minutes, while 36.45% achieved scan time of less than 20 minutes. The data reflects delays at many points from stroke recognition, transport to hospital, ER management, access to imaging, securing of consent for thrombolysis up to administration of rTPA. As sited in a review article, nonrecognition, financial constraints and lack of infrastructure are barriers to thrombolysis (Ghandehari, 2011). The results show that there was no significant difference in the outcome between patients given rTPA within 3 hours and those given within 3 to 4.5 hours, consistent with other literatures. In 5 Japanese hospitals treated within 3 hours and 3 to 4.5 hours, there was no significant difference in NIHSS score, MRS score, the proportions of asymptomatic and symptomatic ICH, and mortality (Morihara et al., 2016). In a pooled analysis of 9 trials, needle time of 4.5 hours increases the chance of improved level of function for all patients across the age spectrum, including the over 80s and across all severities of stroke studied (Lees et al., 2016). In the current 2018 AHA guidelines, if patients present within 3 to 4.5 hours, IV alteplase may now be given to patients >80 y of age, those who took warfarin with INR <1.7, and those with DM (Powers et al., 2018).

# Stroke etiology

The results show that stroke etiology is a significant factor for short term outcome. Theoretically, cardioembolic clots rich in fibrin and red blood cells, are more lysable compared to the more organized platelet-rich atherosclerotic clot. However in our subgroup analysis, majority (67%) of cardioembolic strokes had poor outcome. Majority (98%) of the embolic strokes had moderate to severe etiology. Most strokes were in the MCA territory (83%) with mean baseline NIHSS of 15. Symptomatic ICH was seen in 11%. Twenty six percent (12cases) died in the cardioembolic group, accounting for 71% (12 out of 17) of overall mortality. In this group, the high baseline NIHSS and higher rate of sICH probably account for the poor outcome among them. In a prospective study done among Chinese, unfavourable outcome was shown following thrombolysis with cardioembolic strokes. Symptoms were more severe at onset (mean NIHSS15) and had increased rate of sICH, as in our study (Wang et al., 2015). Atrial fibrillation causing cardioembolic stroke is associated with poorer stroke outcomes (Saposnik et al., 2013). In our study, 18 (40%) of the cardioembolic cases had documented atrial fibrillation and 2 had congenital heart diseases.

# Intake of antiplatelet/ anticoagulants

In the literature, dual antiplatelet usage before rTPA treatment or antiplatelet use within the first 24 hours of rTPA treatment increases the risk of rTPA related HT. In a meta-analysis, antiplatelet intake

was not associated with a higher risk of sICH and worse outcome (<u>Tsivgoulis et al., 2017</u>). In our study, none of the 8 patients who took antiplatelet or anticoagulant as monotherapy prior to rTPA had symptomatic ICH. 1 patient who took Clopidogrel had asymptomatic ICH, however had a poor outcome due to the right ICA infarct. According to current guidelines, IV alteplase is recommended for patients taking antiplatelet drug monotherapy before stroke. For patients taking direct thrombin inhibitors or direct factor Xa inhibitors, alteplase may be given once platelet count, aPTT, INR, and other tests are normal or when the patient has not received a dose of these agents for 48 hours (<u>Powers et al., 2018</u>).

## Hemorrhagic Conversion

Hemorrhagic transformation (HT) significantly affects short-term outcome. While asymptomatic hemorrhage, which is more common, has no effect on the prognosis or shows positive association with clinical outcome, symptomatic ICH predicts poor outcome (Navarro et al., 2014). With a lower dose of 0.6mg/kg, overall rate of HT is 14.01% (15 cases), majority of whom are asymptomatic (9 out of 15 cases).

In accord with the NINDS trial, ICH was categorized as symptomatic versus asymptomatic. With a lower dose of 0.6mg/kg, overall rate of HC is 14.01% (15 cases), majority of whom are asymptomatic. Extracranial bleeding include 3 patients who had UGIB and 2 patients with gum bleeding which were uncomplicated. The rate of minor extracranial bleeding is lower in our study than in NINDS trial (23%).

Other adverse events include 2 cases of gum bleeding among the subgroup. (The other 3 patients who had UGIB and gum bleeding did not have hemorrhagic conversion at all.) Twenty percent of the patients with HC had good outcome. Three (3) patients with asymptomatic hemorrhages had poor outcome due to malignant infarct whereas 6 patients died due to sICH. The rate of sICH is same with the NINDS trial (6.4%).

# Mortality

In western literatures, in-hospital mortality for acute ischemic stroke is approximately 5% to 12%. The overall mortality rate in our study is higher at 15.88% (17 cases), however, is almost similar to the Philippine study on rTPA at 14.6% (Navarro et al., 2018). The mortality due to sICH in our study is very high at 100%. Symptomatic ICH significantly affects outcome. Symptomatic ICH contributes to 35% of overall mortality. The rate of symptomatic ICH (5.6%) is almost the same with the NINDS study and other literatures. However, the mortality rate in this group is higher at 100% compared to the NINDS study. This may reflect the capacity of the institution to address complications of sICH.

#### CONCLUSIONS AND RECOMMENDATIONS

Our data indicate favorable discharge outcomes of intravenous thrombolysis administered to stroke patients. A high baseline NIHSS, cardioembolic stroke etiology, and presence of sICH are seen in patients with poor outcome. The rate of sICH is consistent with other literature, however our study has a higher mortality rate for this group. Mortality is high primarily due to malignant infarct (47%), sICH (35%), and BAO (24%).

There is still great room for improvement regarding stroke management, by giving rtpa to more patients and by giving it faster. The study reflects the capacity of the institution and perhaps the capacity of our nation to address acute stroke and thrombolysis complications. Current stroke care is patchy with few centralized areas of excellence unevenly distributed in the country, with majority of its population unable to access it. Additional infrastructure, equipment, and manpower, and stronger interdepartmental and inter-agency coordination is needed and can be strongly addressed in the national level and local government units, and with the collaboration of the public and private sector.

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#### **AUTHOR CONTRIBUTIONS**

The author conducted the research from the beginning to the end of the study.

#### **FUNDING STATEMENT**

No funding has been received to conduct this study.

#### DATA AVAILABILITY STATEMENT

No data are available for this study.

# CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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