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Haoran Liu Date

Safety And Efficacy of Direct Oral Anticoagulants Versus Warfarin for the Treatment of Left Ventricular Thrombus

By

Haoran Liu
Master of Science in Public Health

Biostatistics and Bioinformatics

_____

Zhengjia Chen, Associate Professor
Thesis Advisor

_____

Xiangqin Cui, Associate Professor
Reader

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Haoran Liu

B.S.
Fudan University
2018

Thesis Committee Chair: Zhengjia (Nelson) Chen, Associate Professor

Reader: Xiangqin Cui, Associate Professor

An abstract of
A thesis submitted to the Faculty of the
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2020

Abstract

Safety And Efficacy of Direct Oral Anticoagulants Versus Warfarin for the Treatment of Left Ventricular Thrombus

By Haoran Liu

Background: A left ventricular thrombus (LVT) is blood clot in the left ventricle with defined margins which blocks the blood vessel. Warfarin is the primarily used medication for LVT as current guidelines but need routine monitoring while direct oral anticoagulants (DOACs) are also attractive options. For now, clinical experiments for comparation between warfarin and DOACs are not enough.

Method and Materials: This study included 50 patients (19 to 87 years old) with a diagnosis of LV thrombus by ICD-9 or ICD-10 who were prescribed a DOAC or warfarin and the patients were followed through any visits to Emory University Hospital and Emory University Hospital Midtown. T-test, chi-square test, Fisher exact test, logistics model and GLM model were used for statistical analysis.

Results: In the multivariate analysis, the odds ratio of resolving thrombus within 6 months of DOAC group was 2.29 higher than the Warfarin group, the chance of transient ischemic attack after thrombus of DOAC group was 0.075 lower than Warfarin group, but the results were both not significant.

Conclusion: Though DOAC has better treatment effect on resolve the thrombus within 6 months compared with warfarin to some degree, which is not significant from the p-value and ROC analysis due to other factors like sample size. We need more patients to be enrolled in in the future research to get a more convincible result.

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CONTENTS

1.INTRODUCTION

A left ventricular thrombus (LVT) is blood clot in the left ventricle with defined margins which blocks the blood vessel and are distinct from the endocardium[1]. Most of LVT cases are related to ischemia, while the rest are due to non-ischemic causes such as dilated and stress induced cardiomyopathy[2]. However, in both ischemic and non-ischemic settings, LVT complicates LV systolic dysfunction and may lead to thromboembolic complications such as cerebrovascular accidents and acute anterior myocardial infarction[3]. Ischemia and reduced ejection fraction are common setting in an anterior myocardial infraction (AMI), which are also the most famous risk factors of the LVT development[4]. The most common method to diagnose LVT currently is the echocardiography, such as two-dimensional Echocardiography[5].

Without systemic anticoagulation, the risk of embolization from an LVT within three months may be as high as 10-20% [6]. However, bleeding complications are not rare when using the systemic anticoagulation[7]. Despite the risks, no randomized controlled trials have evaluated the safety and effectiveness of anticoagulation for LVT. Due to the lack of available data, guidelines on the most appropriate anticoagulant treatment regimens and duration are based mainly on case reports, expert opinions and epidemiological data. Although current guidelines primarily recommend the use of vitamin K antagonists, such as warfarin, the use of direct oral anticoagulants (DOACs) may be an attractive option considering the use of warfarin need to be monitored routinely. In terms of duration of treatment, there is no consensus amongst guidelines, as

recommendations range from three to six months[8-11].

The purpose of our study is to make a comparison between DOACs and warfarin on their safety and efficacy for the treatment of LVT. We are interested in two major objectives: for the primary objective, whether there exists any difference in the proportion of patients with the resolution of thrombus within 6 months of initial diagnosis between the two treatments (DOACs vs Warfarin); for the secondary objective, whether there exists any difference on the incidence of ischemic stroke or major bleeding in patients being treated with DOACs versus warfarin using ICD-9 and ICD-10 codes. To accomplish the primary objective, we used two-sided Mantel-Haenszel test to compare the proportions between the two groups and employed Logistics regression model in multivariable analyses. For the secondary objective, we used the two sample student's t-test to compare the difference in frequency between the two group and General linear model (GLM) in multivariable analyses.

In the remainder of this thesis, we will describe in Methods details of the primary and secondary objectives. In statistics analysis, models will be presented to examine adjusted efficacy of treatment (DOACs vs Warfarin) considering the other covariates. In discussion and conclusion, we will discuss key results to draw conclusions about the safety and efficacy of DOACs versus warfarin for the treatment of left Ventricular thrombus.

2. METHODS AND MATERIALS

The data used for analysis are from a multi-center, retrospective chart review including patients older than 18 years old with a diagnosis of LV thrombus based on ICD-9 or ICD-10 diagnosis codes who were prescribed a DOAC or warfarin and the patients enrolled in this study were followed through any visits to Emory University Hospital and Emory University Hospital Midtown. Data were collected using data Warehouse and EeMR. The data were split into two groups depending on the type of anticoagulation treatment received: DOAC or warfarin.

2.1 Patients and observation parameter.

The dataset included 50 patients (19 to 87 years old), DOAC(N=13) and Warfarin(N=37). Demographics (Age, DOB, Gender, Race), Clinical characteristics (Height, Weight, SCr, CrCl), Type of anticoagulation and dose prescribed, Ejection Fraction at diagnosis, Previous stroke, Atrial Fibrillation, Antiplatelet and anticoagulant medications (based on discharge home medication list), Events (LV thrombus at 6 months, Major bleeding , Stroke or TIA) were recorded to provide evidence on control of covariates in the data analysis.

2.2 Statistical Analysis

2.2.1 Descriptive analysis

We first made descriptive analysis for all variables collected as summary statistics. Continuous variables were presented as means, standard deviation, and range. Binary

and categorical variables were summarized with frequencies and percentages. All the variables were checked on their missingness. Decriptive analysis were also conducted for the two groups separately, DOAC and warfarin.

2.2.2 Univariate and Multivariate Regression Analysis.

First, we wanted to find the difference between the DOAC group and warfarin group and to find if there were any covariates have significant association with the two groups. For the primary objective, the proportion of patients with the resolution of thrombus within 6 months of initial diagnosis (Yes vs No) was estimated with 95% CI assuming a binomial distribution among each of the two groups (DOACs vs Warfarin), respectively.

Then we would like to detect whether any covariates are significantly associated with the primary objective (LV thrombus at 6 months). The proportions were compared between the two groups (DOACs vs Warfarin) using Fisher's Exact test (if the data finalizes with <5 in a group) or two-sided Mantel-Haenszel test (if the data finalizes with >5 in a group). Logistics regression model was further employed in the multivariable analyses to estimate the adjusted efficacy of treatment (DOACs vs Warfarin) on resolution of thrombus within 6 months of initial diagnosis (Yes vs No) after adjusting for other factors. The full model was shown here:

Logit (primary objective=YES) = $\beta_0 + \beta_1 I_{group=DOAC} + \sum \beta i * xi + \varepsilon$ $\quad \varepsilon \sim iid\ N(0, \sigma^2)$

(The reference group is Warfarin group and x_i were all the covariates in the dataset)

In the full model we just added all the covariates in the model and kept the covariate about the treatment group in the final model when doing model selection.

For the secondary objectives, incidence of ischemic stroke or transient ischemic attack (TIA) in patients being treated with DOACs or warfarin using ICD-9 and ICD-10 codes was estimated as frequency and compared between the two groups using two sample student's t-test. General linear model (GLM) was further used in the multivariable analysis to estimate the adjusted efficacy of treatment (DOACs vs Warfarin) on incidence of ischemic stroke or transient ischemic attack (TIA) after adjusting for other factors. The full model was shown here:

Y (chance of TIA after thrombus) = $\beta_0+\beta_1$Group $+\sum \beta i * xi + \varepsilon$ $\quad \varepsilon \sim iid\ N(0, \sigma^2)$

(x_i were all the covariates in the dataset)

In the full model we just added all the covariates in the model and kept the covariate about the treatment group in the final model when doing model selection.

Similarly, t-test and GLM was used to determine and test the incidence of major bleeding using ICD-9 and ICD-10 codes between the two groups among all critical bleeding sites as well as each site, respectively. All the models were used a backward variable selection method with an alpha =.20 removal criteria. The significance level was set at 0.05 for all tests.

2.3 ROC Analysis

In the last part of method, we used a ROC analysis to figure out whether the results and methodology from univariate were solid or not. Two ROC plots were made for the primary objective and secondary objective.

The SAS statistical package version 9.4 (SAS Institute, Inc., Cary, North Carolina) was used for data management and analysis.

3. RESULTS

3.1 Results of Descriptive analysis

The descriptive statistics for patients' characteristics and clinical symptoms were shown in the **Table 1a** and **Table 1b**. From the table, we could see 50 patients are divided into two treatment groups: Warfarin (74.0%) and DOAC (26.0%), specifically, 14% patients used Apixaban and 12% patients used Rivaroxaban. It's reasonable since warfarin was most widely clinically used anticoagulant nowadays.

For characteristics, the mean age of patients was 54.1 with range 19 to 87 years old. After 40 years old, people tended to have a higher incidence of thrombus and the age of trend went down currently.

The mean BMI was 28.11 with range 16.8 to 39.2. Mean height of patients was 172.73 cm with range 157 to 188 cm.70 percent of patients were Black and others were Caucasian. We could see no significant difference in gender with 27 males (54%) and 23 females (46%).

For past ischemia thrombus history, 34% patients had experience with ischemic and 66% did have.。In terms of renal function test, mean Serum Creatinine（SCr）was 1.31 and mean Creatinine clearance(CrCl) was 28.11(standard deviation = 40.49). Higher CrCl and lower SCr were better symptoms for renal function. As for Ejection fraction, mean value was 23.52 with range 10 to 55. 26% patients had atrial fibrillation which will not only reduce the cardiac output, affected the pumping function of the heart, but also produced thrombus. In our study, 38% patients did not have the resolution of thrombus within 6 months, 68% patients' thrombus resolved within 6 months. We noticed only 3 patients had TIA after Thrombus and none of the patients had major bleeding.

3.2 Results of Univariate analysis

3.2.1 result of univariate analysis group by treatment group

The **Table 2.** showed the result of univariate analysis group by the treatment group. We could see that the mean age from patients in the DOAC group is 60.85 compared with 51.73 from Warfarin group, with the p-value 0.085, which is not significant at significance level of 0.05, but suggestive. It indicates that that the two treatment groups have a potential age difference.

For our primary objective, no significant difference between two treatment group with LV Thrombus resolved within in 6 months: Warfarin 64.86% versus DOAC 53.85 with a p-value 0.481 generated from two-sided Mantel-Haenszel test. For our secondary objective TIA after thrombus, though none of the patients in the DOAC group suffered

a stroke, only 8.11% percent of patients with TIA after thrombus was also a small probability event. No significant association was established between treatment group on primary and secondary objective.

3.2.2 result of univariate analysis group by primary objective

The **Table 3.** showed the result of univariate analysis group by the primary objective LV thrombus revolved within 6 months. The atrial fibrillation was significant associated with the proportion of patients with LV thrombus resolved within 6 months with a p-value 0.018. 47.37% patients had a higher atrial fibrillation without thrombus resolved compared with 12.9% patients with thrombus resolved. This result was consistent with the fact that people with atrial fibrillation often caused a thrombus. When patients recovered from atrial fibrillation, they had a better chance to resolve LV thrombus.

There was a strong association between age and whether LV thrombus revolved within 6 months with p-value 0.002. The mean age in the LV thrombus resolved group was 48.47 compared with 62.84 in LV thrombus non-resolved group, indicating that younger patients have better chance to recover from thrombus after received the treatment.

3.3 Results of Multivariate analysis

3.3.1 Logistic regression model for primary objective

The **Table 4.** showed the result of logistic regression for the primary objective LV thrombus resolved within 6 months about the information of estimated coefficients,

their significance and p-value. After a backward selection, our final model was:

Logit(primary objective=YES) = $\beta_0 + \beta_1 I_{group=DOAC} + \beta_2 Age + \beta_3 Height + \beta_4 Weight + \beta_5 CrCl + \beta_6 BMI + \beta_7 Ejection\_Fraction + \varepsilon$ $\varepsilon \sim iid\ N(0, \sigma^2)$

The model showed that the odds ratio of resolving thrombus within 6 months of DOAC group was 2.29 higher than the Warfarin group with other covariates constrained which indicated the DOAC has a better effect on resolving the LV thrombus than Warfarin but the result was not significant. As age went up one unit, the log odds of primary objective would decrease 0.2367 which indicated older people has lower chance to recover after treatment. Relative high ejection fraction, Height and BMI also helped increase the chance of resolving the thrombus. While the odds ratio would decrease when patients' CrCl and Weight increased.

3.3.2 Generalized linear model for secondary objective

The **Table 5.** showed the result of generalized linear regression for secondary objective. Since none of the patients has major bleeding, we only took TIA after Thrombus into consideration. After a backward selection, our final model was:

Y(chance of TIA after thrombus)=$\beta_0+\beta_1 Group+\beta_2 Age+\beta_3 Ischemic\_thrombus+\beta_4 Ejection\_Fraction + \beta_5 other\_antiplatelets+ \varepsilon$ $\varepsilon \sim iid\ N(0, \sigma^2)$

The model showed that the chance of TIA after thrombus of DOAC group was 0.075 lower than Warfarin group which indicated the DOAC has better treatment effect on stroke than Warfarin but the difference was not significant. As age went up 10 years the chance of TIA after thrombus would only increased 0.033 which was not significant. In

terms of ejection fraction, rather low ejection fraction could lower the chance of stroke. Patients with history of ischemic thrombus got really a high chance of TIA after thrombus which was 0.366 higher than patients

3.4 Results of ROC analysis

From **Figure 1a.** we could see the result of the ROC analysis for primary objective LV thrombus resolved within 6 months, which was not significant between the treatment group. The **Table 6a.** showed that the AUC was 0.545, indicating the result was not solid since the AUC was closed to 0.5.

From **Figure 2b.** we could see the result of the ROC analysis for secondary objective after Thrombus, which was not very significant between the treatment group. The **Table 2b.** showed that the AUC was 0.638, indicating the result was not very solid since though the AUC was larger than 0.5 but not too much.

The result from the ROC analysis were along with the result from the univariate analysis.

4. CONCLUSION

From descriptive and univariate analysis, we draw a conclusion that age is an important issue for both primary outcome and secondary outcome. As age goes up the chance of recovery from LV thrombus within 6 months decreases, the chance of TIA after

thrombus increases.

From the result of the multivariate analysis, we draw a conclusion that patients who used DOAC to help resolve thrombus will have better recover rate compared to Warfarin group within 6 months which is the primary objective we take into consideration on their treatment effect. Also, people in DOAC group will have lower risk to infect with TIA after thrombus compared with people in Warfarin group. Though we get the result that DOAC do have better effect compared with Warfarin in both models from multivariate analysis, the p-value of the covariate of the group itself in the model is not significant, which is along with the result in univariate analysis and ROC analysis.

5. DISCUSSION

In this study, we explored the efficacy of warfarin and DOACs on treatment of the LVT thrombus by univariate and multivariate analysis after dividing patients into two groups. Then, we validated the analysis results by ROC analysis.

Since our outcome for primary objective is a binary result and the observations are independent of each other, we choose to use a logistics regression in the multivariate analysis. Also, the logistic regression does not need a linear relationship among all the variables and the residual does not have to fulfill the normal distribution, nor does the

homoscedasticity.

As for limitations, our sample size is not very large since we enroll only 50 patients in this study and some of the cases is very rare for our interested objectives. For example, none of the patients has the symptom of major bleeding and only 3 patients have TIA after Thrombus which does not help much with specifying the treatment effect of the DOAC and Warfarin group. Also, this sample size is not relatively large for a logistics regression to get a proper result. Since we have 7 covariates in our model and the proportion of LV Thrombus resolved within in 6 months is 62 percent, the proper sample size for this study should be 113 patients. In the model selection, we used a backwards selection and kept the variable about the treatment group in the model, but its p-value is not very significant. I think we need to involve more patients into research to double-check the outcome and get a more convincible result in the future study.

6.REFERENCE

1. Delewi R, Zijlstra F, Piek JJ. Left ventricular thrombus formation after acute myocardial infarction. *Heart*. 2012;98(23):1743–1749. doi:10.1136/heartjnl-2012-301962
2. Mir J, Raheel Jahangir J, Asfandyar Q, et al. Left ventricular thrombus in patients with acute anterior wall myocardial infarction. J Ayub Med Coll Abbottabad 2014; 26: 491–495.
3. Kontny, F., Dale, J., Abildgaard, U., & Pedersen, T. R. (1997). Randomized trial of low molecular weight heparin (dalteparin) in prevention of left ventricular thrombus formation and arterial embolism after acute anterior myocardial infarction: the Fragmin in Acute Myocardial Infarction (FRAMI) Study. Journal of the American College of Cardiology, 30(4), 962-969.
4. Keren, A., Goldberg, S., Gottlieb, S., Klein, J., Schuger, C., Medina, A., ... & Stern, S. (1990). Natural history of left ventricular thrombi: their appearance and resolution in the posthospitalization period of acute myocardial infarction. Journal of the American College of Cardiology, 15(4), 790-800.
5. Haugland, J. M., Asinger, R. W., Mikell, F. L., Elsperger, J., & Hodges, M. (1984). Embolic potential of left ventricular thrombi detected by two-dimensional echocardiography. Circulation, 70(4), 588-598.
6. Habash, F. & Vallurupalli, S. Challenges in management of left ventricular thrombus. *Therapeutic Advances in Cardiovascular Disease* 11, 203–213 (2017).

7. Kuijer, P. M., Hutten, B. A., Prins, M. H., & Büller, H. R. (1999). Prediction of the risk of bleeding during anticoagulant treatment for venous thromboembolism. Archives of internal medicine, 159(5), 457-460.

8. O'Gara, P. T. *et al.* 2013 ACCF/AHA Guideline for the Management of ST-Elevation Myocardial Infarction. *Journal of the American College of Cardiology* 61, e78–e140 (2013).

9. Kernan, W. N. *et al.* Guidelines for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke* 45, 2160–2236 (2014).

10. Ibanez, B. *et al.* 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *European Heart Journal* 39, 119–177 (2018).

11. Abubakar, H., Yassin, A. S. & Shokr, M. Rivaroxaban Used for Treatment of a Left Ventricular Thrombus in a Patient With Nonischemic Cardiomyopathy: *American Journal of Therapeutics* 1 (2018). doi:10.1097/MJT.0000000000000722

7.TABLESAND FIGURES

Table 1a. Descriptive Statistics of Characteristics Variables (Continuous)

Cotinuous Variable	Mean	Median	Minimum	Maximum	Std Dev	Missing
Age	54.1	56.5	19	87	16.42	0
Height	172.73	172	157	188	9.51	1
Weight	84.47	85.9	47	137	19.53	0
Scr	1.31	1.12	0.55	5.04	0.8	0
CrCl	85.2	83.73	9.58	193.65	40.49	0
BMI	28.11	28	16.8	39.2	5.64	1
Ejection Fraction	23.52	20	10	55	11.79	1

Table 1b. Descriptive Statistics of Characteristics Variables (Categorical)

Categorical Variable	Level	N(%)=50
Group	Warfarin	37 (74.0)
	DOAC	13 (26.0)
LV Thrombus resolved 6M	No	19 (38.0)
	Yes	31 (62.0)
Major bleeding	No	50 (100.0)
Stroke/TIA after Thrombus	No	47 (94.0)
	Yes	3 (6.0)
Specific Anticoagulant	Warfarin	37 (76.0)
	Apixaban	7 (12.0)
	Rivaroxaban	6 (12.0)
Ethnicity	Caucasian	15 (30.0)
	Black	35 (70.0)
Gender	Male	27 (54.0)
	Female	23 (46.0)
Ischemic thrombus	Ischemc	17 (34.0)
	non-Ischemic	33 (66.0)
Atrial Fibrillation	No	37 (74.0)
	Yes	13 (26.0)
Antiplatelet/anticoagulant hor	No	22 (44.9)
	Yes	27 (55.1)
	Missing	1
Home Aspirin	No	24 (48.0)
	Yes	26 (52.0)
Other Antiplatelets	none	38 (76.0)
	prasugrel	3 (6.0)
	clopidogrel	8 (16.0)
	ticagrelor	1 (2.0)
Apixaban Rivaroxaban	15 mg daily	2(16.7)
	2.5 mg twice daily	1(8.3)
	20 mg daily	4(33.3)
	5 mg twice daily	5(41.7)
	Missing	37

Table 2. Univariate analysis with treatment group

			Group		P-value
Covariate	Statistics	Level	Warfain N=37	DOAC N=13	
LV Thrombus resolved 6M	N (Col %)	No	13 (35.14)	6 (46.15)	0.481
	N (Col %)	Yes	24 (64.86)	7 (53.85)	
Stroke/TIA after Thrombus	N (Col %)	No	34 (91.89)	13 (100)	0.558
	N (Col %)	Yes	3 (8.11)	0 (0)	
Ethnicity	N (Col %)	Caucasian	9 (24.32)	6 (46.15)	0.14
	N (Col %)	Black	28 (75.68)	7 (53.85)	
Gender	N (Col %)	Male	21 (56.76)	6 (46.15)	0.509
	N (Col %)	Female	16 (43.24)	7 (53.85)	
Ischemic thrombus	N (Col %)	Ischemc	12 (32.43)	5 (38.46)	0.693
	N (Col %)	non-Ischemic	25 (67.57)	8 (61.54)	
Atrial Fibrillation	N (Col %)	No	27 (72.97)	10 (76.92)	1
	N (Col %)	Yes	10 (27.03)	3 (23.08)	
Anticoagulant home med list	N (Col %)	No	17 (47.22)	5 (38.46)	0.586
	N (Col %)	Yes	19 (52.78)	8 (61.54)	
Home Aspirin	N (Col %)	No	19 (51.35)	5 (38.46)	0.424
	N (Col %)	Yes	18 (48.65)	8 (61.54)	
Other Antiplatelets	N (Col %)	none	28 (75.68)	10 (76.92)	0.635
	N (Col %)	prasugrel	3 (8.11)	0 (0)	
	N (Col %)	clopidogrel	5 (13.51)	3 (23.08)	
	N (Col %)	ticagrelor	1 (2.7)	0 (0)	
Age	N		37	13	**0.085**
	Mean		51.73	60.85	
	Median		53	58	
	Min		19	41	
	Max		87	80	
	Std Dev		17.38	11.31	
Height	N		36	13	0.35
	Mean		173.5	170.59	
	Median		172.35	167.6	
	Min		157	157	
	Max		188	182.9	
	Std Dev		9.86	8.43	
Weight	N		37	13	0.371
	Mean		85.95	80.25	
	Median		88.6	78.9	
	Min		47.2	47	
	Max		137	106.3	
	Std Dev		20.38	16.86	
Scr	N		37	13	0.236
	Mean		1.23	1.54	
	Median		1.14	1.08	
	Min		0.55	0.67	
	Max		4.22	5.04	
	Std Dev		0.6	1.21	
CrCl	N		37	13	0.156
	Mean		90.04	71.42	
	Median		84	83.45	
	Min		29.87	9.58	
	Max		193.65	139.25	
	Std Dev		40.6	38.32	
BMI	N		36	13	0.636
	Mean		28.34	27.46	
	Median		29.05	27.9	
	Min		17	16.8	
	Max		39.2	35.6	
	Std Dev		5.98	4.73	
Ejection Fraction diagnosis	N		36	13	0.771
	Mean		23.82	22.69	
	Median		20	20	
	Min		10	10	
	Max		55	55	
	Std Dev		12.11	11.29	

Table 3. Univariate analysis with LV Thrombus resolved at 6M

			Group		P-value
Covariate	Statistics	Level	No N=19	Yes N=31	
Stroke/TIA after Thrombus	N (Col %)	No	17 (89.47)	30 (96.77)	0.549
	N (Col %)	Yes	2 (10.53)	1 (3.23)	
Ethnicity	N (Col %)	Caucasian	7 (36.84)	8 (25.81)	0.409
	N (Col %)	Black	12 (63.16)	23 (74.19)	
Gender	N (Col %)	Male	11 (57.89)	16 (51.61)	0.665
	N (Col %)	Female	8 (42.11)	15 (48.39)	
Ischemic thrombus	N (Col %)	Ischemc	5 (26.32)	12 (38.71)	0.369
	N (Col %)	non-Ischemic	14 (73.68)	19 (61.29)	
Atrial Fibrillation	N (Col %)	No	10 (52.63)	27 (87.1)	**0.018**
	N (Col %)	Yes	9 (47.37)	4 (12.9)	
Anticoagulant home med list	N (Col %)	No	6 (33.33)	16 (51.61)	0.215
	N (Col %)	Yes	12 (66.67)	15 (48.39)	
Home Aspirin	N (Col %)	No	7 (36.84)	17 (54.84)	0.216
	N (Col %)	Yes	12 (63.16)	14 (45.16)	
Other Antiplatelets	N (Col %)	none	16 (84.21)	22 (70.97)	0.848
	N (Col %)	prasugrel	1 (5.26)	2 (6.45)	
	N (Col %)	clopidogrel	2 (10.53)	6 (19.35)	
	N (Col %)	ticagrelor	0 (0)	1 (3.23)	
Age	N		19	31	**0.002**
	Mean		62.84	48.74	
	Median		60	51	
	Min		36	19	
	Max		87	77	
	Std Dev		14.07	15.61	
Height	N		19	30	0.995
	Mean		172.74	172.72	
	Median		172.7	171.1	
	Min		157	157	
	Max		188	188	
	Std Dev		9.4	9.73	
Weight	N		19	31	0.376
	Mean		81.31	86.4	
	Median		77.7	89.1	
	Min		47	47.2	
	Max		137	127	
	Std Dev		22.04	17.92	
Scr	N		19	31	0.932
	Mean		1.33	1.31	
	Median		1.11	1.13	
	Min		0.55	0.61	
	Max		5.04	4.22	
	Std Dev		0.94	0.71	
CrCl	N		19	31	0.303
	Mean		77.59	89.86	
	Median		63.69	88.21	
	Min		9.58	10	
	Max		187	193.65	
	Std Dev		42.41	39.23	
BMI	N		19	30	0.233
	Mean		26.89	28.88	
	Median		26.9	29.55	
	Min		16.8	17	
	Max		39.2	38.6	
	Std Dev		6.05	5.33	
Ejection Fraction diagnosis	N		19	30	0.398
	Mean		21.71	24.67	
	Median		25	20	
	Min		10	10	
	Max		45	55	
	Std Dev		8.42	13.51	

Table 4. Logistics regression model (LV thrombus resolved within 6 months)

Logistic Regression with model selection sls=0.2				
Analysis of Maximum Likelihood Estimates				
Parameter	Estimate	Standard Error	Wald Chi-Square	Pr > ChiSq
Intercept	-126.5	54.5466	5.3803	**0.0204**
Group（ref=Warfarin）	0.8305	1.0476	0.6285	0.4279
Age	-0.2367	0.0758	9.7426	**0.0018**
Height	0.7724	0.3241	5.681	**0.0171**
Weight	-0.6875	0.2925	5.5239	**0.0188**
CrCl	-0.0523	0.021	6.1822	**0.0129**
BMI	2.3137	0.9587	5.8246	**0.0158**
Ejection Fraction diagnosis	0.1809	0.0742	5.9427	**0.0148**

Table 5. Generalized linear regression model (TIA after thrombus)

GLM Model Selection sls=0.2					
Parameter	**DF**	**Estimate**	**Standard**	**t Value**	**Pr > |t|**
		Error			
Intercept	1	0.783094	0.200122	3.91	**0.0003**
Group	1	-0.07466	0.077531	-0.96	0.2999
Age	1	-0.00331	0.002275	-1.46	0.155
Ischemic thrombus	1	-0.36556	0.119504	-3.06	**0.0029**
Ejection Fraction diagnosis	1	-0.00644	0.003504	-1.84	0.0593
Other_Antiplatelets_	1	-0.13258	0.059909	-2.21	**0.0278**

Table 6.a ROC result for primary objective

ROC Association Statistics							
ROC Model	Area	Standard Error	95% Wald Confidence Limits		Somers' D	Gamma	Tau-a
Treatment Group On Priamry Objective	0.545	0.0668	0.4141	0.6759	0.09	0.2255	0.0433

Table 6.b ROC result for secondary objective

ROC Association Statistics							
ROC Model	Area	Standard Error	95% Wald Confidence Limits		Somers' D	Gamma	Tau-a
Treatment Group On Priamry Objective	0.6383	0.033	0.5737	0.7029	0.2766	1	0.0318

Figure 1a. ROC Curve for LV thrombus resolved within 6 months

(an AUC of 0.5 suggests no discrimination**)**

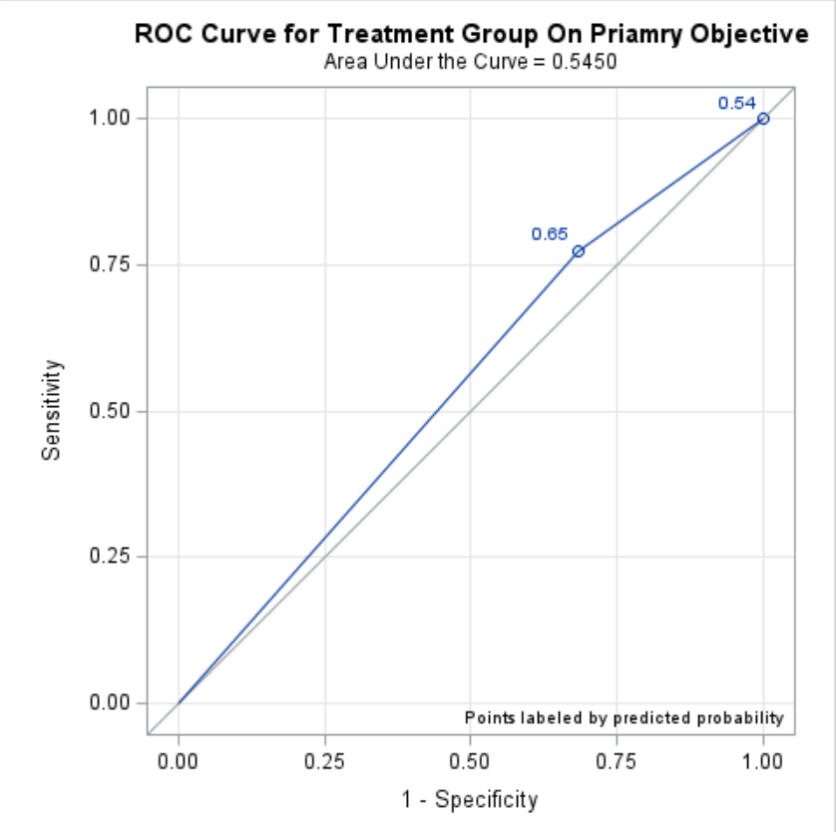

Figure 1b. ROC Curve for TIA after stroke

(an AUC of 0.5 suggests no discrimination**)**