Does Antiplatelet Resistance Testing predict outcomes of Severity of Recurrent Strokes?

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Background

The use of antiplatelet agents such as aspirin, clopidogrel, and aspirin/dipyridamole for secondary stroke prevention is well documented in the literature. However, it is unclear whether switching antiplatelet medications is beneficial in stroke patients who were already on one or more antiplatelet medication prior there stroke1. It is also unclear whether antiplatelet resistance results in increased stroke severity. Our study reviewed whether being antiplatelet sensitive or resistant resulted in differences in stroke severity using the NIHSS.

Methods

This study was a retrospective cross-sectional cohort study of all patients presenting with a new ischemic stroke between 1/2009-12/2011;a total 381patients were included.Study participants were analyzed in groups consisting of those sensitive, resistant and not treated with either clopidogrel or aspirin. The group being treated with both clopidogrel and aspirin was compared to those not being treated with any antiplatelet therapy. Categorical data was compared between groups using Chi-square or Fisher's exact tests as appropriate. Continuous data for age and NIH stroke scale score were not normally distributed and were transformed into rank data (non-parametric). Rank of age and NIH Stroke Scale score were then compared between groups using either the Mann-Whitney U-test or the Kruskal-Wallis test to compare distributions of rank data and the Median Test to compare median values. Spearman correlations were then performed on rank of NIH Stroke Scale score data for all group comparisons displaying significant differences in distribution or medians of rank data to determine the direction and magnitude of the differences.

Table 1: Demographic Characteristics.

Demographic Characteristic	Number (%)
Number	381 (100%)
Female Gender	187 (49.1%)
Diabetes present	127 (33.3%)
Hypertension present	319 (83.7%)
Dyslipidemia present	212 (55.6%)
Heart failure present	24 (6.30%)
Coronary Artery Disease or Prior MI present	148 (38.8%)
Peripheral Vascular Disease present	10 (2.62%)
Carotid Stenosis present	15 (3.94%)
Current Smoking present	59 (15.5%)
Treated with Aspirin	137 (36.0%)
Treated with Plavix	131 (34.4%)
Treated with both Aspirin and Plavix	90 (23.6%)
No Antiplatelet therapy	203 (53.3%)
Aspirin Sensitive	116 (30.4%)
Plavix Sensitive	70 (18.4%)
Continuous Data	**Mean (S.D.)/Median**
Age	72.84 (12.43), 75.00
NIH Stroke Scale Score	6.38 (6.57), 4.00

Table 2: Aspirin Sensitive versus Resistant.

Measure	Aspirin Sensitive	Aspirin Resistant	Sig
Number	116 (100%)	16 (100%)	N/A
Rank of Age (Medians)	152.00	135.50	0.748
Rank of Age (Distributions)	N/A	N/A	0.550
Rank of NIH Stroke Scale Score (Medians)	162.00	162.00	0.862
Rank of NIH Stroke Scale Score (Distributions)	N/A	N/A	0.906
Female Gender number (%)	46 (39.7%)	11 (68.8%)	0.136
Diabetes present number (%)	43 (37.1%)	7 (43.8%)	0.985
Hypertension present number (%)	99 (85.3%)	14 (87.5%)	0.202
Dyslipidemia present number (%)	70 (60.3%)	8 (50%)	0.136
Heart failure present number (%)	7 (6.0%)	2 (12.5%)	0.467
Coronary Artery Disease or Prior MI present number (%)	47 (40.5%)	8 (50.0%)	0.896
Peripheral Vascular Disease present number (%)	4 (3.4%)	1 (6.3%)	0.698
Carotid Stenosis present number (%)	9 (7.8%)	1 (6.3%)	0.700
Current Smoking present number (%)	25 (21.6%)	4 (25.0%)	0.961

Table 3: Plavix Sensitive versus Resistant.

Measure	Plavix Sensitive	Plavix Resistant	Sig
Number	70 (100%)	62 (100%)	N/A
Rank of Age (Medians)	139.50	189.25	0.83
Rank of Age (Distributions)	N/A	N/A	0.173
Rank of NIH Stroke Scale Score (Medians)	116.50	194.50	0.135
Rank of NIH Stroke Scale Score (Distributions)	N/A	N/A	0.049
Female Gender number (%)	33 (47.1%)	28 (45.2%)	0.820
Diabetes present number (%)	24 (34.3%)	28 (45.2%)	0.202
Hypertension present number (%)	59 (84.3%)	55 (88.7%)	0.460
Dyslipidemia present number (%)	45 (64.3%)	37 (59.7%)	0.586
Heart failure present number (%)	4 (5.7%)	6 (9.7%)	0.390
Coronary Artery Disease or Prior MI present number (%)	33 (47.1%)	29 (46.8%)	0.966
Peripheral Vascular Disease present number (%)	6 (8.6%)	0 (0%)	0.018
Carotid Stenosis present number (%)	8 (11.4%)	3 (4.8%)	0.172
Current Smoking present number (%)	14 (20.0%)	8 (12.9%)	0.275

Figure 1: Analysis Diagram for NIH Stroke Scale Score in Aspirin or Plavix Sensitivity Groups

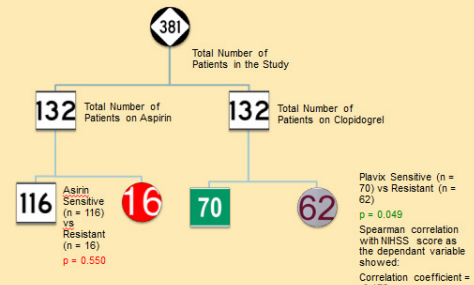
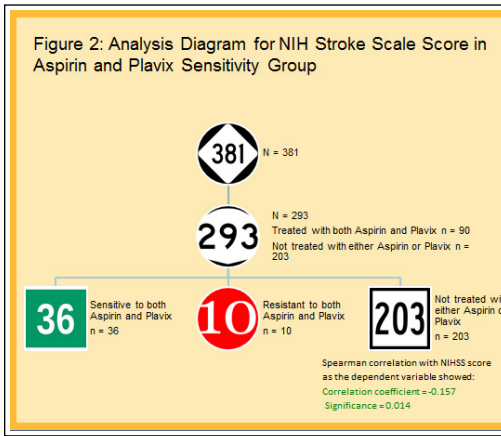


Figure 2: Analysis Diagram for NIH Stroke Scale Score in Aspirin and Plavix Sensitivity Group



Results

The distribution of rank NIHSS scores significantly differed between those sensitive to clopidogrel versus those that were not (p=0.049). No significant difference between median rank NIHSS scores were detected between those sensitive to clopidogrel versus those that were not (p=0.135). A similar finding was not found with aspirin sensitive patients versus those that were not aspirin sensitive (distributions: p=0.906, medians: p = 0.862). Additionally, patients on both aspirin and clopidogrel who were sensitive to both were compared to those that were not sensitive to either and those not treated with either aspirin or clopidogrel, and a direct correlation was detected between increasing NIHSS score and antiplatelet resistance by Spearman correlation test (p=0.014, correlation coefficient = 0.157).

Discussion

Although it remains to be determined if antiplatelet "switching" because of platelet insensitivity results in additional protective benefit in stroke patients, our study shows that clopidogrel appears to result in a decreased stroke severity based on non-parametric ranking of the NIHSS. Prior small studies2,3 showed a similar result with aspirin; however our study did not show a similar finding. Although this was a retrospective study, it does provide some evidence that antiplatelet resistance to clopidogrel results in differences in stroke severity. Additional, prospective studies are needed to better understand this phenomenon.

Conclusion

This is the first study to show an association between clopidogrel platelet sensitivity and stroke severity.

References:
Milionis H, Michel P. Acute ischemic cerebrovascular events on antiplatelet therapy: What is the optimal prevention strategy? Curr Pharm Des. 2012 Dec 26. [Epub ahead of print], Zheng AS, Churilov L, Colley RE, Goh C, Davis SM, Yan B. Association of aspirin resistance with increased stroke severity and infarct size. JAMA Neurol. 2013 Feb 1;70(2):208 -13. doi: 10.1001/jamaneurol.2013.601. , 3. Kim JH, Kim YS, Sohn SI, Cho KH. Biochemical Aspirin Resistance Affect on Stroke Severity in Acute Stroke Patients Who Had Taken Aspirin. J Korean Neurol Assoc. 2011 Nov;29(4):303-308.