AANS/CNS Joint Cerebrovascular Annual Meeting
Los Angeles, California
February 15-16, 2016

Evaluation of Variable Clopidogrel Response by P2Y12 Platelet Function Testing and Subsequent Outcomes in Patients Undergoing Neurointerventional Procedures

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Introduction

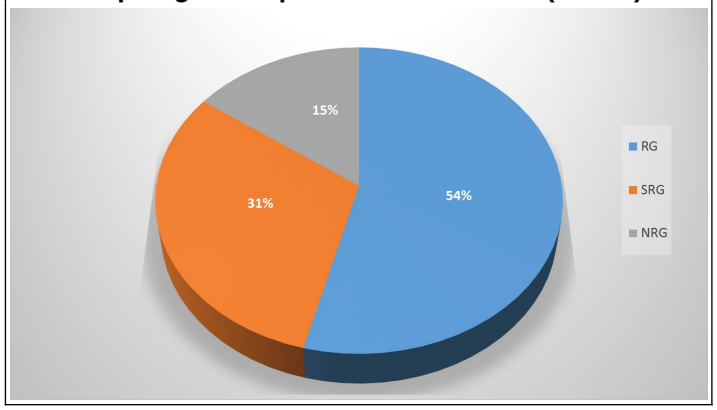
Platelet function testing as a standard of care during neuroendovascular intervention (NI) remains controversial due to limited data on its clinical efficacy. We report outcomes after intracranial and extracranial stenting between variable clopidogrel response groups based on the results of the VerifyNow P2Y12 Assay (Accumetrics, San Diego, California, USA) in P2Y12 reaction units (PRU). At our institution, PRU values $\leq$ 194 are considered therapeutic. Patients who do not intially achieve therapeutic PRUs are either rebolused with clopidogrel until PRUs are therapeutic, or they are switched to another antiplatelet agent.

Methods

- Retrospective, single-center study of consecutive patients who underwent NI stenting from July 2010-June 2015
- Inclusion criteria: documented, preprocedural clopidogrel response assays at the time of stenting
- Primary outcome: quantify the variability of clopidogrel response defined as responder group (RG), subsequent responder group (SRG) and nonresponder group (NRG) and determine the incidence of thrombosis and hemorrhagic complications at 6-month follow-up
- PRU values $\leq$ 194 were considered therapeutic
- Secondary outcomes: identify clinical characteristics associated with assay responsivenesses; further characterize subsequent therapies used in SRG and NRG
- Statistical analysis: descriptive statistics, Fisher's Exact Test with an alpha significance level of 0.05 using SAS software
- Approved by the Institutional Review Board at Virginia Commonwealth University

Results

Clopidogrel Response Classification (N=188)



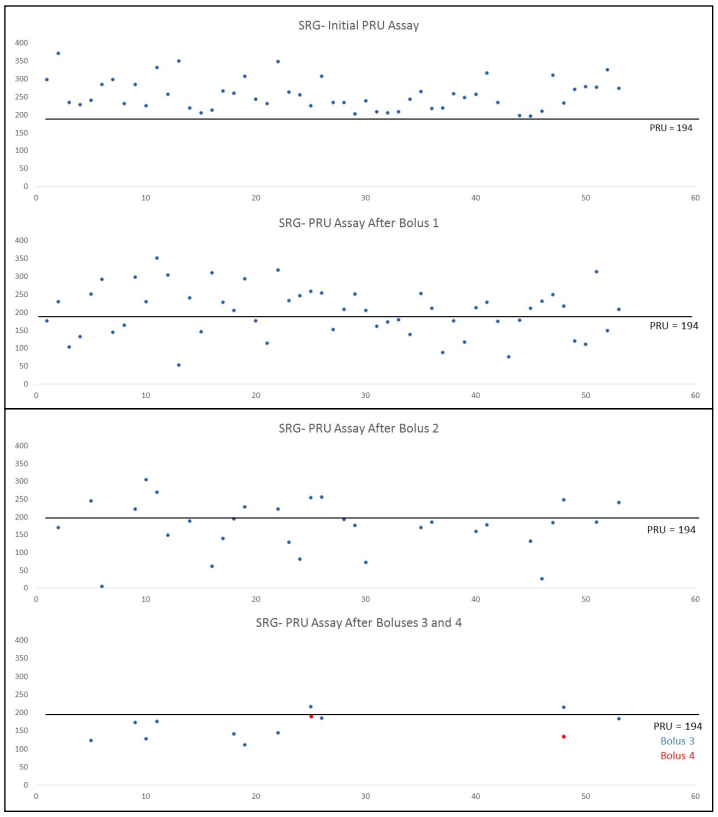
At 6 month follow-up, the thrombotic complication rate per group was significantly increased in the NRG [RG 0/101 (0%), SRG 0/53 (0%), NRG 2/34 (6%), p= 0.02]. No patients experienced a hemorrhagic complication.

	RG (N=101)	SRG (N=53)	NRG (N=34)
Age, mean	62	65	64
Men, n (%)	57 (56)	36 (68)	14 (41)
PPI use, n (%)	23 (22)	11 (21)	10 (29)
Tobacco use, n (%)	44 (43)	19 (36)	8 (24)
Previous Stroke, n (%)	46 (45)	25 (47)	13 (38)
Hypertension, n (%)	82 (81)	46 (88)	20 (59)
Diabetes, n (%)	20 (19)	14 (26)	14 (41)
CAD, n (%)	21 (20)	11 (21)	12 (35)
Hyperlipidemia, n (%)	53 (52)	30 (57)	16 (47)

PPI, proton pump inhibitor; CAD, coronary artery disease
*no characteristics were statistically different between groups

In the SRG, the median total bolus dose was 900 mg, and the median number of boluses was 2. Of the 34 NRG patients, 38% of patients were continued on clopidogrel, 38% were switched to dipyridamole/ASA, and 24% were switched to ticagrelor.

Subsequent Responder Group Analysis



Conclusions

- Approximately 1/3 of patients required additional clopidogrel to achieve therapeutic PRU values.
- Functional outcomes did not differ between RG and SRG patients. Six percent of NRG patients had a thrombotic complication.
- This study is limited due to its retrospective design and population size.
- Prospective studies are needed to provide a better understanding of the clopidogrel dose – outcome relationship in NI stenting procedures.

References

Kass-Hout T, Alderazi YJ, Amuluru K, et al. Intervent Neurol. 2014;3:184-9.