Critical Role of Platelet Inhibition Optimization in Patients Undergoing Intracranial Aneurysm Stent Embolization

Amir Molaie BS; Soleil Ibrahim B.S.; Laura Molina BA; Shane M Burke B.S.; Adel M. Malek MD PhD
Cerebrovascular and Endovascular Division, Department of Neurosurgery
Tufts Medical Center and Tufts University School of Medicine, Boston, MA 02111

CNS 2018 ANNUAL MEETING
HOUSTON, TEXAS
OCTOBER 6-10, 2018

Introduction

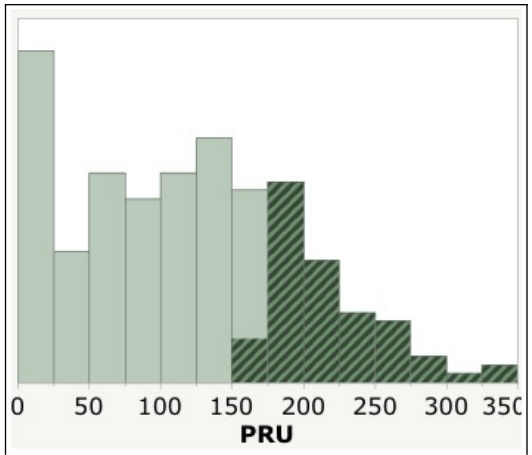
Dual antiplatelet therapy (DAPT) is critical to avoid risk of thromboembolic events in intracranial aneurysm stent treatment (1). However, the prevalence of high on-treatment platelet reactivity, which can contribute to poor outcomes (2,3), remains poorly defined among the cerebral aneurysm patient population.

Characteristic	Median PRU on DOP
All patients started on clopidogrel (*N*=230)	117
Clopidogrel Non- or hypo-responders (*N*= 75)	182
All patients on ticagrelor (*N*=55)	58
All patents on prasugrel (*N*=29)	52

Table comparing inhibition on clopidogrel, ticagrelor, and prasugrel.

Methods

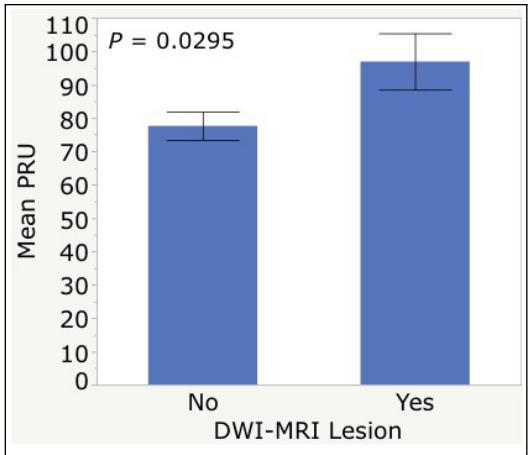
252 patients treated with Neuroform Atlas, LVIS, and Pipeline stents in 265 procedures between 2012 and 2018 were included. Patients were started on daily clopidogrel 75 mg and aspirin 325 mg 7-10 days pre-procedurally and underwent platelet aggregation testing using VerifyNow P2Y12 assay on day of procedure (DOP). Patients found to be inadequately inhibited by clopidogrel (PRU>170) in a pre-op office visit, on DOP, or post-procedure were switched to either ticagrelor 90mg bid, or daily prasugrel 10 mg after loading doses. Procedural thromboembolic ischemia was evaluated using diffusion-weighted brain MRI (DW-MRI) within 24 hours.



Histogram depicting initial PRU among 230 patients started on clopidogrel. Highlighted portion delineates 63 patients with PRU>170.

Results

Patients initiated on clopidogrel (n=230) had PRU=118.2 ± 78 (median 117); 63/230 (27.3%) had PRU >170 to indicate poor P2Y12 inhibition response. However, 75/230 (32.6%) were considered non- or hypo-responders with PRU=186.7 ± 55.5 (median 182) and were switched to an alternate regimen. Hypo-responders switched to ticagrelor had PRU=78.8 ± 61.4 (median 75) and those switched to prasugrel had PRU=57.6 ± 37.9 (median 54). All patients on prasugrel (n=29) had PRU=53.8 ± 42.0 (median 52.1), showing significantly greater inhibition compared to patients started or switched to ticagrelor (n=55) PRU=70.1 ± 57.0 (median 58). Greater platelet inhibition on DOP was significantly associated with absence of DW-MRI lesions on post-procedural MRI (PRU 77.6 vs. 96.9, p <0.03).



Presence of restricted diffusion on 24-hour DWI-MRI was significantly associated with high PRU.

Discussion

In our series of cerebral aneursym stent embolizations, 32.6% of patients showed an inadequate response to clopidogrel, prompting a change in DAPT regimen. This compares with findings in the cardiovascular literature, which reports a rate of clopidogrel unresponsiveness in up to 49.5% of the population (4). The relationsip between elevated platelet reactivity and thromboembolic complications is controversial and not well understood. However, identification and correction of persistent platelet activity prior to procedures has been shown to improve outcomes (5). Although it needs to be balanced against the risk of hemorrhage, maintaining lower periprocedural PRU may reduce the risk of ischemic events related to stent placement.

Conclusions

Inadequate platelet inhibition by clopidogrel is seen in a third of aneurysm patients undergoing intracranial stenting. Cautious pre-procedural testing and diligent selection of alternate agents with repeat testing on day of procedure can help lower thromboembolic ischemic events in this patient population.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Describe the importance of platelet inhibition in decreasing thromboembolic complications during aneurysm stent embolization, 2) Discuss strategies for identifying and mitigating high on-treatment platelet reactivity, and 3) Compare the effectiveness of different anti-platelet regimens.

References

1.Ries T, Buhk JH, Kucinski T, et al. Intravenous administration of acetylsalicylic acid during endovascular treatment of cerebral aneurysms reduces the rate of thromboembolic events. Stroke 2006;37:1816-21.
2. Aoun SG, Welch BG, Pride LG, White J, Novakovic R, Hoes K, et al. Contribution of whole platelet aggregometry to the endovascular management of unruptured aneurysms: an institutional experience. Journal of neurointerventional surgery. 2017;9(10):974-7.
3. Fifi JT, Brockington C, Narang J, Leesch W, Ewing SL, Bennet H, et al. Clopidogrel resistance is associated with thromboembolic complications in patients undergoing neurovascular stenting. AJNR American journal of neuroradiology. 2013;34(4):716-20.
4. Mallouk N, Labruyere C, Reny JL, Chapelle C, Piot M, Fontana P, et al. Prevalence of poor biological response to clopidogrel: a systematic review. Thrombosis and haemostasis. 2012;107(3):494-506.
5. Adeeb N, Griessenauer CJ, Foreman PM, Moore JM, Shallwani H, Motiei-Langroudi R, et al. Use of Platelet Function Testing Before Pipeline Embolization Device Placement: A Multicenter Cohort Study. Stroke. 2017;48(5):1322-30.