Correlation of platelet reactivity testing and CYP2C19 metabolizer status in patients undergoing endovascular neurosurgical procedures

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BACKGROUND

- Patients undergoing endovascular neurosurgical procedures such as intracranial/extracranial stent placement or flow-diverting stents are indicated to receive dual-antiplatelet therapy (DAPT)
- Clopidogrel is the most used P2Y12 inhibitor for DAPT, and is a prodrug activated by the CYP2C19 hepatic enzyme
- Response to clopidogrel therapy can be assessed using the VerifyNow Platelet assay (measured in platelet reactivity units [PRUs])
- Alternatively, a predicted phenotype can be derived from genotyping the *CYP2C19* gene.
- At the University of Florida (UF) Health, platelet reactivity testing is routine in patients undergoing endovascular neurosurgeries, but *CYP2C19* genotyping is less frequent

OBJECTIVE

To correlate *CYP2C19* genotype and phenotype results with platelet reactivity test results of patients undergoing endovascular neurosurgical procedures.

METHODS

- Data were collected for patients who had *CYP2C19* genotyping ordered by the neurosurgical department from Jan-Dec 2020
- These included demographics, *CYP2C19* genotype and phenotype, type of neurosurgical intervention, antiplatelet therapy (including dose/agent changes), and platelet reactivity test results
- Platelet reactivity tests were only included if they were drawn appropriately and at steady state
- Patients with two functional alleles of *CYP2C19* were considered normal metabolizers (NM), patients with one or two increased activity alleles were rapid (RM) or ultra-rapid metabolizers (UM), respectively, and patients with one or two no function alleles were intermediate (IM) or poor metabolizers (PM), respectively

RESULTS

Table 1. Demographics of all patients

Demographics	No. of patients (%)
Total Patients	41
Female sex	23 (56)
Average Age (stdev)	64 (± 18)
Self-reported race	
European ancestry	31 (76)
African ancestry	5 (12)
Other	5 (12)
Diagnosis	
Unruptured aneurysm	21 (51)
Vessel stenosis	15 (37)
Subarachnoid hemorrhage (SAH)/stroke	5 (12)
Intervention	
Flow diversion	17 (41)
Carotid stenting	10 (24)
Stent assisted coiling	6 (15)
None	4 (10)
Initial P2Y12 inhibitor therapy	
Clopidogrel 75 daily	36 (88)
Clopidogrel 75 QOD	1 (2)
Ticagrelor 90 mg BID	2 (5)
None	2 (5)
Final P2Y12 inhibitor therapy	
Clopidogrel 75 daily	22 (54)
Clopidogrel 75 QOD	6 (15)
Clopidogrel 37.5 daily	3 (7)
Ticagrelor 90 mg BID	7 (17)
None	3 (7)

Figure 1. Platelet reactivity test results per CYP2C19 phenotype

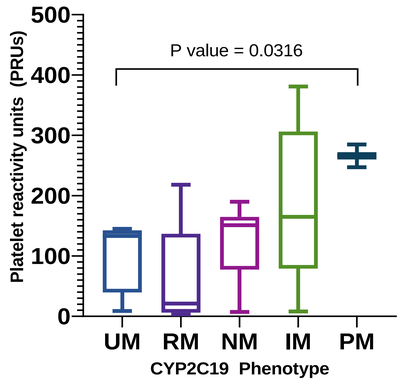


Table 2. CYP2C19 Phenotype and PRUs Resulting in Medication Changes

CYP2C19 Phenotype	Platelet reactivity response (based on PRU)	No. of patients (%)	Medication changes based on PRU
UM n = 4	Hyper	1 (25)	1
	Optimal	3 (75)	0
RM n = 14	Hyper	4 (29)	4
	Optimal	7 (50)	2
	Nonresponder	1 (7)	1
	N/a	2 (14)	0
NM n = 15	Hyper	2 (13)	2
	Optimal	8 (53)	0
	N/a	5 (33)	0
IM n = 5	Hyper	1 (20)	1
	Optimal	2 (40)	0
	Nonresponder	2 (40)	1
PM n = 3	Nonresponder	2 (67)	1
	N/a	1 (33)	0

Figure 2. Clopidogrel non-responder PRU trends after medication changes (n=3)

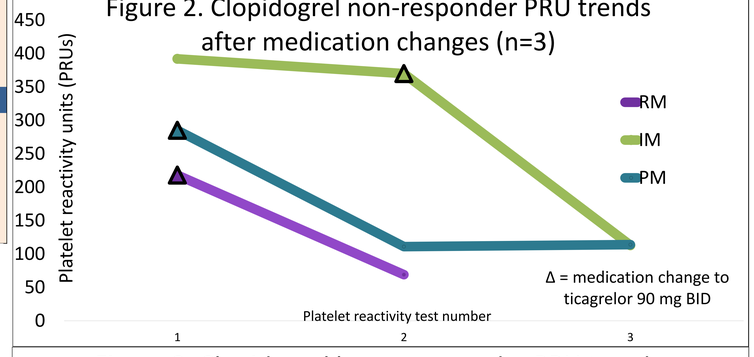
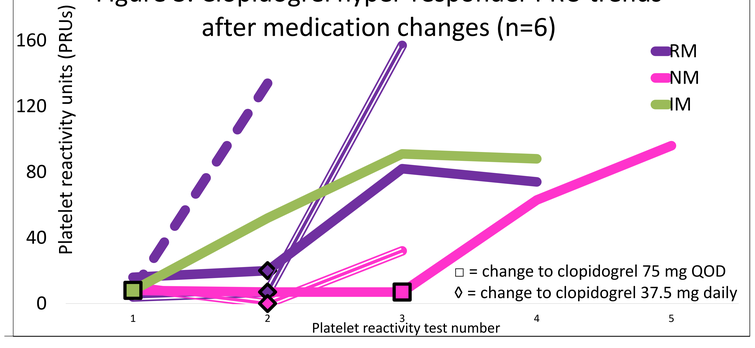


Figure 3. Clopidogrel hyper-responder PRU trends after medication changes (n=6)



METHODS CONT.

- Patients were categorized as non-responders to clopidogrel if their platelet reactivity tests were >204 PRUs, hyper-responders if their platelet reactivity tests were <20 PRUs, and optimal responders if their platelet reactivity fell between 20-204 PRUs
- If a patient had more than one steady-state platelet reactivity test, their test values were averaged.
- All patient charts were assessed for omeprazole and glycoprotein IIb/IIIa inhibitor use during the time of platelet reactivity testing
- One-way ANOVA was calculated for PRUs based on phenotype
- Trends in PRUs were tracked for patients who received platelet reactivity testing both before and after a medication change

DISCUSSION

- Overall, platelet reactivity testing does appear to correlate with CYP2C19 metabolizer status in most patients undergoing endovascular neurosurgical procedures
- Further studies are required in this patient population to confirm this finding, as this patient cohort was small

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