### Background

Dual antiplatelet therapy with aspirin and clopidogrel is associated with reduced morbidity and mortality in patients with acute coronary syndromes (ACS). It is recommended to treat ACS patients with both drugs even before their coronary anatomy has been delineated. In patients subsequently requiring coronary artery bypass grafting (CABG) this early treatment with clopidogrel frequently delays surgical intervention until 5 days after the last drug dose. We have not found any literature substantiating this arbitrarily decided upon 5 day waiting period. We investigated platelet aggregation properties in ACS patients scheduled for CABG. We hypothesized that clopidogrel effect on platelets aggregation may last less than 5 days.

### Material and Methods

All consenting patients scheduled for CABG underwent daily platelet reactivity testing after receiving 600 mg of clopidogrel at the time of catheterization. Platelet reactivity testing using (PU) was performed with point of care VerifyNow® P2Y12 assay. The VerifyNow® P2Y12 is a rapid assay that test platelet activity over 3 min and uses of the combination of ADP and prostaglandin E1 (PGE1) to directly measure the effects of clopidogrel on the P2Y12 receptor. ADP is used to maximally activate the platelets by binding to the P2Y1 and P2Y12 platelet receptors, while PGE1 is used to suppress the ADP-induced P2Y1-mediated increase in intracellular calcium levels. Twenty-four hour interval was given between sampling and administration of. Of 34 patients recruited, 3 patients crossed over to induced P2Y-mediated increase in intracellular calcium levels. Twenty-four hour interval was given between sampling and administration of. Of 34 patients recruited, 3 patients crossed over to induced P2Y-mediated increase in intracellular calcium levels. Twenty-four hour interval was given between sampling and administration.

### Results

Of 34 patients recruited, 3 patients crossed over to medical management strategy, 1 patient died while awaiting surgery. In additional 1 patient VerifyNow® could not be done due to low hemocrit. On data remaining 29 patients (41 females, 34% with diabetes) was analyzed. Most of the patients (83%) were awaiting surgery. In additional 1 patient VerifyNow® could not be done due to low hemocrit. On data remaining 29 patients (41 females, 34% with diabetes) was analyzed. The most of the patients (83%) were awaiting surgery. In additional 1 patient VerifyNow® could not be done due to low hemocrit. On data remaining 29 patients (41 females, 34% with diabetes) was analyzed. The most of the patients (83%) were awaiting surgery.

### Discussion

We have investigated temporal trends in recovery of clopidogrel reduced platelet aggregation in patients loaded with 600 mg of clopidogrel who are scheduled to undergo CABG surgery. In these patients surgery is routinely postponed for at least 5 days after the last clopidogrel dose. Experimental foundation for such waiting approach is lacking. Platelet reactivity was studied with a commercially available point of care assay VerifyNow®, an ADP mediated activation of the P2Y12 receptors on the platelet. Several studies have compared VerifyNow® with other laboratory measurements of platelet reactivity and found these tests to be equivalent (1,2).

### Conclusion

1. Majority of the patients (55%) have less than 30% platelet inhibition in 48 hours after loading with 600 mg of clopidogrel.
2. Older patients are more likely to have recovery of platelet function, as compared to the younger counterparts. The discovery is consistent with the finding of Gremmel et al, that ADP-inducible platelet reactivity shows a pronounced age dependency in the initial phase of antplatelet therapy with clopidogrel (3). In addition, there were more diabetics (41% vs. 17%) amongst patients with early recovery of platelet function, but this difference was not statistically significant (p=0.272, Table 1), possibly due to the small sample size. Interestingly, patients who recovered platelet reactivity in 48 hours also had higher creatinine levels than the rest of the study cohort (1.6±2.7 vs. 0.9±0.15 mg/dl), consistent with reported decreased platelet responsiveness to clopidogrel in patients with chronic renal failure (7). There may be other mechanisms affecting clopidogrel responsiveness: inadequate absorption or metabolism of the drug (4,5); genetic polymorphisms affecting either drug metabolism, mainly by cytochrome P450 and cytochrome P2C19, or the pharmacologic target of clopidogrel (5,6). Which mechanism is predominant in patients scheduled for CABG remains to be established.

Regardless of the platelet reactivity parameters there was no difference in the blood product requirements after the surgery. This finding requires further investigation, in a study of a larger cohort.