Prevalence and Impact of High Platelet Reactivity in Chronic Kidney Disease: Results from the ADAPT-DES Registry

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Background: Chronic Kidney Disease (CKD) is associated with an increased risk for stent thrombosis and adverse events following percutaneous coronary intervention (PCI). High platelet reactivity (HPR) is also an independent correlate of thrombotic events post PCI. Although CKD modulates platelet function, the impact of CKD on HPR remains controversial, and whether or not HPR confers a differential risk for MACE between CKD and non-CKD patients is unknown.

Methods: We performed a post-hoc analysis of the ADAPT-DES registry, which included 8,583 patients (8,449 of whom had baseline serum creatinine measures). We performed a post-hoc analysis of the ADAPT-DES registry, which included 8,583 patients (8,449 of whom had baseline serum creatinine measures).

Results: We compared the frequency and impact of HPR on MACE between CKD and non-CKD patients.

Conclusions: While HPR is more common among those with CKD, this association appears largely attributable to confounding risk factors that are more prevalent in these patients. The incremental impact of HPR on MACE is similar among those with and without CKD.

Table 1. Adjudicated Events to 1-Year

<table>
<thead>
<tr>
<th>Event at 3, 6, 12 mths</th>
<th>PRU</th>
<th>99th Percentile</th>
<th>Adjusted HR (95% CI)</th>
<th>P-Value</th>
<th>CI 95% Lower Boundary</th>
<th>CI 95% Upper Boundary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent thrombosis (definite/probable)</td>
<td>1.8% (12)</td>
<td>0.6% (4)</td>
<td>3.18 (1.03, 9.87)</td>
<td>1.2% (15)</td>
<td>0.5% (20)</td>
<td>2.34 (1.34, 4.08)</td>
</tr>
<tr>
<td>Cardiac death or MI</td>
<td>7.3% (48)</td>
<td>5.6% (39)</td>
<td>1.31 (0.86, 1.99)</td>
<td>4.2% (123)</td>
<td>2.9% (117)</td>
<td>1.47 (1.24, 1.69)</td>
</tr>
<tr>
<td>MACE*</td>
<td>10.9% (71)</td>
<td>8.1% (56)</td>
<td>1.38 (0.95, 1.99)</td>
<td>7.1% (206)</td>
<td>5.8% (232)</td>
<td>1.24 (1.03, 1.56)</td>
</tr>
<tr>
<td>MACE2**</td>
<td>7.3% (48)</td>
<td>5.6% (39)</td>
<td>1.31 (0.86, 1.99)</td>
<td>4.4% (127)</td>
<td>2.9% (119)</td>
<td>1.52 (1.18, 1.95)</td>
</tr>
</tbody>
</table>

TCT-7

Impact Of Early Versus Late Clopidogrel Discontinuation On Stent Thrombosis Following Percutaneous Coronary Intervention With First-And Second-Generation Drug-Eluting Stents

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Background: Premature discontinuation of antiplatelet therapy after percutaneous coronary intervention is known to predict stent thrombosis (ST). We aimed to compare the impact of early versus late antiplatelet therapy discontinuation on ST in patients receiving first- and second-generation drug-eluting stents (DES).

Methods: A total of 6587 patients undergoing PCI with DES were analyzed, of which 5580 received 1st-generation DES (Cypher or Taxus) and 2007 received 2nd-generation DES (Xience or Promus). Patients were categorized into timing of clopidogrel discontinuation within 1 year (never, <3 months, 3-12 months) and ≥1 year (3-12 months, and <1 year, respectively).

Results: In patients with 2nd-generation DES, 536 (11.7%) had clopidogrel discontinued, 137 (3.8%) within first 3 months and 363 (7.9%) at 3-12 months. Cumulative 1-year ST rates were 1.0%, 3.5%, 3.6% (p < 0.001) for never, <3 months, 3-12 months discontinued, respectively. (Figure A) In patients with 2nd-generation DES, 214 (11.9%) had clopidogrel discontinued, 44 (4.7%) within first 3 months and 120 (5.9%) at 3-12 months. Cumulative 1-year ST rates were 0.1%, 5.4%, 5.4% (p < 0.001) for never, <3 months, 3-12 months discontinued, respectively. (Figure B).

Conclusions: While newer drug eluting stent (DES) promote more favorable vascular healing, the optimal duration of dual antiplatelet therapy (DAPT) after implantation with 2nd generation drug-eluting coronary stents remains underdetermined. We aimed to test whether 6-month DAPT would be non-inferior clinical and angiographic outcome to 12-month DAPT after implantation of Zotarolimus-eluting stent (ZES) and biolimus-eluting stent (BES).

Methods: This is a prospective, double-randomized, open-label, multicenter trial to compare clinical events between 6-month DAPT and 12-month DAPT (in a 1:1 ratio), and to demonstrate the non-inferiority of BES compared with ZES stents (in 1:1 ratio), angiographically. Currently, 1055 patients were randomly assigned. The primary end point was a major adverse cardiac events (MACE) at 12 months. Optical coherence tomography (OCT) at 6 month was performed in 30 patients of each group. The primary endpoint was MACE, secondary end points are target lesion failure, in-segment LL at 12 months, and neointimal hyperplasia (NIH) by OCT at 6 month.
Results: Currently, clinical follow-up was available in 628 patients and angiographic follow-up in 526 patients (608 lesions). The primary endpoints were not statistically different between the 6- and 12-month DAPT groups, including MACE (4.6 vs. 3.4%; p = 0.49) and stent thrombosis (0.0 vs. 0.3%; p = 0.71), and MACE (3.4 vs. 4.6%; p = 0.49) and stent thrombosis (0.3 vs. 0.0%; p = 0.71), according as type of stents (BES vs. ZES, respectively). The secondary endpoints also were not significantly different between the 6- and 12-month DAPT groups, including target lesion failure (2.0 vs. 1.6%; p = 0.53), in-segment LL (mm) at 12 months (0.09±0.37 vs. 0.05±0.39; p = 0.61). Similar results were shown between stents type. And NIH CSA (mm2) at 6month between BES and ZES were 0.38±0.28, 0.45±0.32, respectively (p=0.41).

Conclusions: Six-month DAPT did not increase the risk of MACE, stent thrombosis, target lesion failure, and LL at 12 months after implantation of drug-eluting stents compared with 12-month DAPT. The 2nd generation DES including BES and ZES are comparably efficacious. Our results need to be confirmed in larger trials and further follow up data.

TCT-9

Racial Disparity With On-Treatment Platelet Reactivity In Patients Undergoing Percutaneous Coronary Intervention

Lakshmana Pendyala1, Salem Badr1, Israel Barbash1, Fang Chen2, Kenneth Kent3, Racial Disparity With On-Treatment Platelet Reactivity In Patients Undergoing Percutaneous Coronary Intervention

Laura Mauri1, Donald Catlin2, Anthony Gershlick3, Dean Kereikides4, Joseph Massaro5, Ian T. Meredith5, John A. Ormiston5, Philippe G. Steg5, Robert Yeh6,7

Background: On-treatment platelet reactivity to clopidogrel is variable and in part genetic dependent. In African American (AA) patients, the relation between on-treatment platelet reactivity to clopidogrel and the factors that influence this interaction are unknown. The present study aims to evaluate on-treatment platelet reactivity to clopidogrel in AA patients and its interaction to race and CYP2C19*2 loss of function mutation.

Methods: The study cohort included 289 consecutive patients presenting for percutaneous coronary intervention (PCI) who were entered into a prospective, observational registry. High on-treatment platelet reactivity (HTPR) was defined as P2Y12 reaction units (PRU) ≥208 with VerifyNow P2Y12 assay and >50% by vasodilator-stimulated phosphorylase phosphorilation assay platelet reactivity index (VASP PRI) measured 6-24 hours post-procedure. CYP2C19*2 (rs4244285) genotype was analyzied by real-time polymerase chain reaction.

Results: The prevalence of HTPR by both PRU (56% vs. 35%, p = 0.003) and VASP PRI (67% vs. 45%, p = 0.002) is more common in AA compared to Caucasians, respectively. AA patients had higher on-treatment, mean PRU (207±110 vs. 163±102; p = 0.002) and VASP PRI (49±26 vs. 38±25; p = 0.004). AA also had a higher prevalence of CYP2C19*2 allele carrier status compared to Caucasians (43% vs. 29%; p = 0.04). AA race (p = 0.008) and CYP2C19*2 allele status (p = 0.02) independently had significant effects on PRU and VASP. Multivariable logistic regression analysis has shown that both CYP2C19*2 allele carrier status and AA race were independent correlates of HTPR for PRU ≥208.

Conclusions: AA patients undergoing PCI not only have a higher prevalence of HTPR to clopidogrel but also have higher CYP2C19*2 allele carrier status compared to Caucasians. Careful selection of antiplatelet agents should be considered in an AA population at higher risk for ischemic complications.

TCT-10

Differences Between US and non-US Cohorts after PCI and Dual Antiplatelet Therapy: Patient Characteristics, Randomization

Laura Mauri1, Donald Catlin2, Anthony Gershlick3, Dean Kereikides4, Joseph Massaro5, Ian T. Meredith5, John A. Ormiston5, Philippe G. Steg5, Robert Yeh6,7

Background: Comparative effectiveness studies may seek to enroll geographically diverse populations to enhance generalizability. We compared enrollment, randomization, drug and device utilization between US and non US patients across a large international trial.

Methods: The Dual Antiplatelet Therapy (DAPT) Study is a double-blind randomized trial designed to compare durations of DAPT after PCI with stents respect to clinical events. Patients were enrolled between August 2009 and July 2011. At 12 months, eligible patients were randomized to receive placebo+aspirin or thienopyrimidine-aspirin through study endpoint (30 months). We compared patient and procedure characteristics, patterns of stent and medication choice, compliance with antiplatelet therapy, and randomization rates, between patients enrolled in the US and other countries.

Results: The DAPT Study enrolled 26,194 patients treated with drug-eluting (N = 23,210) or bare metal (N=2,984) stents, 23,495 in the US (90%) and 2,699 in other countries: UK 629, Poland 388, Germany 372, Romania 312, Hungary 271, New Zealand 239, Australia 197, France 101, Canada 96, and Czech Republic 94. Non-US patients were more likely to be male, current smokers, present with acute coronary syndrome, receive bare metal vs drug-eluting stents, clopidogrel vs prasugrel, and aspirin doses ≤100 mg daily (each p < 0.001). At 12m, non-US patients were more likely to be DAPT compliant (94.7 vs 89.2%; p < 0.001). Non-US patients were more likely to be randomized (65% vs 43%; p < 0.001), even after adjusting for baseline characteristics (OR = 2.27; p < 0.001).

Conclusions: Within the DAPT Study, non-US patients were more likely to be compliant with study procedures, independent of patient characteristics. Regional variation in patient characteristics, compliance, and practice patterns observed in broadly inclusive clinical trials allows for the evaluation of interactions between these factors and treatment effectiveness.

Bare Metal and Drug-Eluting Stents

Moscone West, 3rd Floor, Room 3024

Tuesday, October 29, 2013, 1:00 PM–3:00 PM

Abstract nos: 11-21

TCT-11

Abstract Withdrawn