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6th International Conference on

CARDIOLOGY

June 29, 2023 | Webinar

Aparajita Kumar, Curr Res Cardiol,
ISSN: 2368-0512 | Volume 10

Received date: 22-03-2023 | Accepted date: 25-03-2023 | Published Date: 07-07-2023

Optimal duration of dual antiplatelet therapy after angioplasty and the DAPT score

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Background: The benefits of dual antiplatelet therapy with aspirin and a P2Y12 receptor antagonist (DAPT) in Acute coronary Syndrome and those undergoing percutaneous coronary interventions has been clearly established as a standard of care. However,the duration of use of dual antiplatelet therapy after Percutaneous coronary intervention is evidence based,and the optimal duration is often arbitrary and unclear. The ACC/AHA and the European Society of Cardiology guidelines published between 2011 and 2014 recommend a minimal 12 month of dual antiplatelet therapy in most patients with DES implantation. Prolongation of dual antiplatelet therapy beyond one year of Percutaneous Coronary Intervention may be beneficial by way of decreased incidence of atherothrombotic events including recurrent Myocardial infarction or stent thrombosis,but at the cost of increased risk of major or minor bleeding. The PEGASUS TIMI 54 trial showed that addition of the P2Y12 antagonist ticagrelor to low dose aspirin in patients 1 to 3 years after a myocardial infarction significantly reduced rate of major adverse cardiovascular outcomes. Aspirin monotherapy alone has at best modest antiaggregatory activity on platelets,especially in the acute phase in high risk patients to prevent ischaemic events;since it only inhibits the cyclooxygenase pathway whilst having no effect on the adenosine diphosphate P2Y12 receptor.Combination therapy results in more robust inhibition of platelet aggregation .This was established by the CHARISMA trial, which demonstrated significant benefit in reduction of myocardial infarction,stroke,repeat revascularisation,and death in patients at high risk of ischemic events /established vascular disease who received clopidogrel alongwith aspirin. Continual of dual antiplatelet therapy beyond one year after index PCI is common despite the dilemma of benefit/risk ratio to the patient. The PARIS registry showed that in a cohort of 5031 patients, 43%of patients with ACS and 57% of those undergoing elective PCI remained on DAPT at the end of 2 year followup.It has been proposed that DAPT score can aid in individualising antiplatelet therapy,and identify those who actually benefit from prolonged regimen of dual antiplatelets.

Objective: To evaluate the rationale for continual of Dual antiplatelet therapy beyond one year after index PCI, and to correlate it with the DAPT score.

Methods: 500 patients who underwent PCI at our centre with a final diagnosis of ST Elevation Myocardial Infarction ,Non ST Elevation acute coronary syndrome, or stable ischemic heart disease,and were compliant with antiplatelets were evaluated and followed up for at least one year post PCI.The type of thienopyridines prescribed in addition to aspirin was noted for each patient ;alongwith any concurrent oral Vitamin K antagonists/novel oral anticoagulants prescribed.Exclusion criteria remained those patients who were lost to followup,those who expired in hospital, and those who underwent only plain old balloon angioplasty and were not stented. The DAPT and HASBLED scores were used as risk stratification methods to assess ischaemic and bleeding risks. The indication for percutaneous intervention, size of stents used,and whether it was a drug eluting stent or bare metal stent was noted. History of restensosis or prior stenting or CABG was taken.Prexisting comorbidities such as diabetes,hypertension,hypercholesterolemia,prior myocardial infarction ,prior cardiac surgery and previous cerebrovascular accident or transient ischaemic attack were taken into account.The primary endpoints were non fatal recurrent Myocardial infarction,stent thrombosis,non fatal ischemic CVA ,repeat revascularisation or death.The primary safety endpoints included major and/or minor bleeding,and the need for blood transfusion.

Results: Of all the eligible patients receiving dual antiplatelets followed up, 292(58.4%) were diabetic, 233 (46.6 %)were hypertensive, 267 (53.4%) were dyslipidemic while 62(12.4%) were smokers.292(58.4%) had presented as STEMI,73(14.6%) had NSTEMI, while 24(4.8%) had restenosis,1 patient had subacute stent thrombosis and remaining 47(9.4%) had stable angina, 32(6.4%) had Left Main Coronary Artery disease,55(11%) had bifurcation lesions,16(3.2%) underwent Saphenous Vein Graft stenting, 5(1%) had chronic total occlusion; and 100 patients had stents longer than 28 mm.103(20.6%) had 2 or more stents.41(8.2%)were on aspirin monotherapy at the end of 1 year after PCI,9(1.8%) were on clopidogrel alone,1 patient was on prasugrel monotherapy ,while majority 212(42.4%) were on a combination of aspirin and clopidogrel;7 (1.4%)were on

aspirin and ticagrelor,14/2.8% were on aspirin plus prasugrel .Furthermore,3(0.6%) patients were on concurrent oral Vitamin K antagonists(warfarin/acenocoumarol) and 1 patient was on NOAC(dabigatran) for thromboprophylaxis of atrial fibrillation/ intracardiac thrombus/recurrent CVA/previous prosthetic valve.96(19.2%) had a HASBLED score of 3 or more,while 28/5.6% patients had HASBLED score higher than 4. 234/46.8% had a DAPT score greater than or equal to 2.35/7% had LV ejection fraction <45%,and 23/4.6% had prior history of CHF.60/12% had a prior myocardial infarction,10/2% had prior CVA,19/3.8% had recent MI. 12/2.4% had bleeding complications within one year.36(7.2%) had prior PTCA,15(3%)had undergone prior CABG. 96/ 19.2% had MACE, of which 46/9.6% underwent repeat PCI,27/5.4% had recurrent MI,7 patients (1.4%) had stent thrombosis,7/1.4% patients had ischemic CVA within one year of PCI,9/1.8% expired.6/1.2% had history of Subdural hematoma,8/1.6% patients had intracranial bleed,13/2.6% patients had GI bleeding;while 7/1.4% had non GI bleeding like epistaxis/hematuria.14/2.8% patients required blood transfusions .None of the patients had fatal bleed.23/4.6% had underwent emergency surgeries,and 24 patients underwent elective surgeries. Of the 41 patients on aspirin monotherapy,8(19.5%) had MACE,of which 26 underwent repeat PCI,and 3 expired,whilst 11/2.2% patients had bleeding;as opposed to 9 patients on clopidogrel alone,of which 2 had MACE(22.2%),including one death, and 5/7% patients had GI bleed.

Discussion: Dual antiplatelet therapy in patients treated with coronary stent implantation reduces the risk of ischemic events and stent thrombosis in atherosclerotic cardiovascular disease.The current recommended period of dual antiplatelets based on observational data after DES implantation is 12 months;whilst after BMS implantation is 1 month. The PCI CURE analysis showed that dual antiplatelet therapy upto 12 months in patients with NSTEMI treated with BMS reduced ischemic events compared to aspirin monotherapy.The Dual Antiplatelet Therapy trial also demonstrated that patients who underwent stenting with DES who were treated on extended dual antiplatelet regimen had 0.7% absolute reduction in late stent thrombosis ,2 % absolute risk reduction in MI and 1.6% risk reduction in MACE after index PCI , with a fundamental tradeoff of 1.2% increased risk of moderate/ severe bleeding. Furthermore,post hoc analyses from other studies implicated greater benefit with prolonged intensive antiplatelet therapy.A weighted risk-benefit analysis by the ERC of prior studies of patients revascularised with DES showed 6 lesser myocardial infarctions and 3 fewer stent thromboses,but 5 additional major bleeding per 1000 patients on prolonged DAPT annually.Prolonged DAPT regimen was defined as 18 to 36 months after DES implantation.The results of our analysis shows almost comparable rates of Major Adverse Cardiovascular outcomes in both arms of single and dual antiplatelet therapy,with greater incidence of bleeding observed on dual antiplatelet regimen.Lifelong DAPT in patients undergoing DES revascularisation is unwarranted, as the risks of bleeding and cost of prolonged treatment outweighs potential reduction in stent thrombotic events.Nevertheless,12 months of DAPT is reasonable after DES implantation, although treatment should be individualised based on presence of ischemic risk factors,the anatomical complexity of lesion,and the type of stent implanted. Abbreviated thienopyridine therapy may be considered in the event of significant bleeding risks;including concurrent oral vitamin K antagonist usage,and anticipated surgery.

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3. Laura Mauri, Dean J. Kereiakes, Robert W. Yeh, Priscilla Driscoll-Shempp, Donald E. Cutlip,,P. Gabriel Steg, M.D., Sharon-Lise T. Normand, Eugene Braunwald et al: Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents.

Biography

Aparajita is an Associate Consultant, Clinical & Preventive Cardiology at Medanta Medicity, Gurugram. Her expertise lies in all aspects of clinical and preventive cardiology, echocardiography and has a keen interest in cardiac research. She has worked as Senior Research Fellow at AIIMS Delhi, and has also worked as Consultant Non Invasive Cardiology at Columbia Asia Hospital, MS Ramaiah Narayana Hrudalaya as well as Max Hospital, Dehradun in the past. She has been an International Speaker at various Cardiology conferences, and is an AHA certified ACLS & BLS Instructuctor. She has completed Research To Publication course by UCMS California, and is also an International Associate, American College of Cardiology.

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