OUTCOMES WITH LONGTERM DUAL ANTIPLATELET THERAPY AFTER CORONARY ANGIOPLASTY

Ashok Kumar Arigonda, K. Nagendra Prasad, O. Hareesh , R. Keerthika

ABSTRACT :

Introduction: *The optimal duration of dual antiplatelet therapy (DAPT) after drug-eluting stent (DES) implantation is an important, unanswered question. This study was designed to evaluate the association of varying durations of DAPT on clinical outcomes after DES implantation for the treatment of coronary artery disease.*

Methods: *Registry is maintained about the follow up of patients on DAPT therapy post percutaneous transluminal coronary angioplasty (PTCA) and the complications are noted in the follow up period between December 2015and May 2016 in NIMS hospital. Results were analyzed using appropriate Statistical tests.*

Results: *The number of evaluated patients was 127 with median age of 62 years. There were 27 females in them. Mean DAPT score was 1.68, with majority in the score range of one or two. Mean follow up period was 5.92 years (1 to 15 years). Among 127patients only 4 patients had complications, 3 of them had chronic stable angina and one had ischaemic stroke with no bleeding complication.*

Conclusion: *DAPT beyond one year has benefits in terms of low associated complications and low incidence of coronary events.* .

Key words: *Dual antiplatelet therapy, long term follow up, PTCA.*

INTRODUCTION

In patients with obstructive coronary artery disease who undergo percutaneous coronary intervention (PCI) to improve symptoms, stents and in particular drug-eluting stents (DES), are used in the majority. Stent thrombosis is an uncommon but serious complication of coronary artery stenting that often presents as death and is almost always accompanied by myocardial infarction (MI), usually with ST-segment elevation [1]. Dual antiplatelet therapy (DAPT) combining aspirin with an adenosine diphosphate receptor inhibitor has significantly reduced the incidence of ischaemic events, including stent thrombosis, after percutaneous coronary intervention, and is thus strongly recommended by international practice guidelines [2]. However, less clear has been the optimal duration for which DAPT should be recommended, especially in the context of a drug-eluting stent (DES) implantation, where previous reports have implicated an association with increased late stent thrombosis events after DAPT has been stopped. In addition, this issue is further influenced by the exposure of the patient to an increased risk of bleeding while on DAPT. Since the duration of DAPT is still largely driven by individual physician and/or patient preference rather than evidence, we sought to determine the outcomes of longer duration of DAPT in practice by analyzing the complication rate retrospectively.

Article received on 2 July 2016, published on 30 July 2016.
A. Ashok Kumar[1] , K. Nagendra Prasad[1],O.Harish[1], R. Keerthika[1]
[1]Senior Resident, Department of Cardiology, NIMS, India
Corresponding author: Ashok Kumar,
Email:ashokari@gmail.com

MATERIALS & METHODS

Patients who underwent successful implantation of at least one DES during their index PCI were followed up in the period between December 2015 to May 2016 in our cardiology unit, in NIZAMS INSTITUTE OF MEDICAL SCIENCES, Hyderabad hospital and among them those who were discharged on DAPT were considered eligible for analysis. Patients who had intermittent DAPT interruptions or not continued the regimen were excluded from the analysis. The DAPT score ranges from -2 to 10 and is made up of the following factors: age, diabetes status, smoking status, PCI or MI history, presence of chronic heart failure or LEFT VENTRICULAR EJECTION FRACTION(LVEF)<30% and index procedure characteristics: MI at presentation, vein graft PCI, and stent diameter [1]. Data on baseline demographic, clinical, angiographic, and procedural characteristics during the index PCI, as well as the occurrence of death, myocardial infarction, and the need for repeat revascularization, non-cardiac complication like cerebrovascular accident were collected If patients

underwent subsequent repeat revascularization (either PCI or CABG) data were collected whenever possible. We analyzed the data using the follow up from the index procedure stratified by use of DAPT score.

RESULTS:

Total number of cases was 127. Baseline clinical parameters are provided in Table 1. Majority of them were males (78.74%). 77.1% are hypertensives and 74.8% are diabetics. 15.74% are smokers. 7.875% had prior MI. MI at index procedure in 9.44%.

Table 1 : Demographic features of the study population.

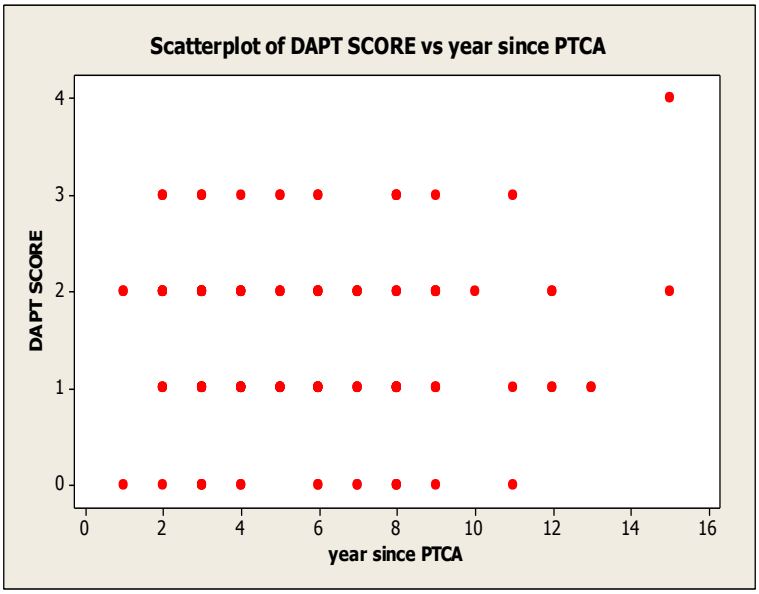
Parameter	No (%)
Total no.	127
Male	100 (78.74%)
Female	27(21.26%)
DM	95(74.8%)
HTN	98(77.17%)
Smoker	20(15.74%)
Prior MI or PCI	10 (7.87%)
MI as presentation at procedure time	12(9.44%)

Median age of these patients were 62 years and followed them for mean of 5.92 years (Table 2, Fig 1). We had 61 (48.03%) patients in 1 to 5 years follow up, 55 (43.3%) patients for6 to 10 years follow up and 11 (8.66%) patients for 11 to 15 years follow up.

Table 2: Details of DAPT score and years of follow up.

VARIABLE	Mean	SD	Median	Min-Max
Age	60.82	9.2	62	35 – 80
DAPT score	1.48	0.8	1	1 – 4
Year since PTCA	5.92	3.0	6	1 - 15

Fig 1 : Scatter plot of DAPT score showing the distribution of DAPT score during the follow up years.



4 patients had complications (3.15%). Three patients had CSA and one patient had CVA. The details of age, DAPT score and years of follow up were mentioned in Table 3.

Table 3 : Details of the patients who had complications during follow up.

Complication	No. Case	Mean Age	DAPT Score	Average Years of follow up	Sex
CSA	3	51	1.67	7.33	2 (M),1 (F)
CVA	1	66	1	4	1 (F)

In Table 4 , the distribution of DAPT score among the 127 patients and complications were mentioned. Complications were noted in patients with DAPT score of one or two, but not in higher scores.

Table 4 : Complications according to DAPT score.

DAPT score	No of patients	Complication
Zero	16 (12.6%)	Nil
One	52(40.9%)	Two (one CVA, one CSA) (1.6%)
Two	45(35.4%)	Two (CSA) (1.6%)
Three	14(11%)	Nil
Four	01(0.8%)	Nil

DISCUSSION:

All patients who undergo percutaneous coronary intervention (PCI), including those treated with balloon angioplasty without stenting, receive dual antiplatelet therapy (DAPT), which is the combination of aspirin and a P2Y12 receptor blocker to reduce the risk of (MI) or cardiovascular death. DAPT likely decreases the risk of these ischemic events by preventing stent thrombosis and by lowering the risk of adverse events consequent to plaque rupture at sites remote from the stented location [3].

The rationale for the use of DAPT, as opposed to antiplatelet monotherapy, is derived from the known tendency of circulating blood to clot in the presence of many metals. This period of risk decreases after the metal portion of the stent is endothelialized. More intense antiplatelet therapy (DAPT) lowers the risk of stent thrombosis compared with aspirin alone. Patients who may be reasonable candidates for less than one year of DAPT include those at relatively high bleeding risk: a history of transient ischemic attack or stroke, age ≥75 years, propensity to bleed (eg, recent trauma or surgery, recent or recurrent gastrointestinal bleeding, active peptic ulcer disease, severe hepatic impairment), body weight <60 kg, or concomitant use of medications that increase risk(oral anticoagulants or nonsteroidal anti-inflammatory drugs).

The optimal duration of DAPT after implantation of DES is unclear. Based upon the initial randomized clinical trials of the first generation DES, the Food and Drug Administration and ACC/AHA Guidelines initially recommended DAPT for 6 months with paclitaxel-eluting (Taxus) stents and 3 months with Sirolimus eluting stents. Studies suggested patients who received 1 year of clopidogrel therapy after DES implantation had better survival at 2 years follow up compared to those who received therapy for a shorter duration therapy. Current guidelines now recommend at least 1-year of DAPT for patients who receive a DES if they are not at high risk for bleeding [4].

Subsequently, several reports revealed conflicting information regarding the benefit of DAPT beyond one year after DES implantation. Other recent data from the PRODIGY and EXCELLENT trials suggest that shorter DAPT duration may be safe in selected patients [5]. Since the duration of DAPT is still largely driven by individual physician and/or patient preference rather than evidence, we sought to determine the outcomes of longer duration of DAPT in practice by analyzing the complication rate retrospectively. We studied the patients retrospectively who were on the DAPT following the initial years following the first generation DES, latter with second generation DES.

In our study, we had 127 patients, mostly distributed with DAPT score between 0 to 2. We followed these patients for an average of 5.92 years. We observed complications in 4 patients (3.15%). Three patients had CSA and three patients had chronic stable angina. There were no obvious bleeding complications related to DAPT. This shows the safety of DAPT beyond one year also.

The DAPT trial is the largest of the randomized trials that have compared longer- with shorter-duration DAPT after DES placement. Other randomized trials such as PRODIGY, DES-LATE, and ARCTIC-Interruption did not show a decrease in ischemic events with longer therapy [6]. The DAPT trial showed that overall ischemic event rates and stent thrombosis were lower with 30 rather than 12 months of DAPT after stenting, the rate of MI not related to stenting was also lower (1.8 versus 2.9 percent; hazard ratio [HR] 0.59; $p<0.001$). This difference accounted for 55 percent of the total reduction in MI with prolonged DAPT. However, the risk of bleeding was increased [7]. Whereas in our study cardiovascular complication being low without any observed bleeding complication despite of long term DAPT.

At a lower DAPT score, there is a greater increase in bleeding and smaller reduction in ischemia. At a higher score, there is a greater reduction in ischemia and small increase in bleeding. The DAPT investigators concluded that patients with a score < 2 have greater harm than good from continued therapy beyond 12 months, while those with a score of 2 or more derive benefit from treatment for an additional 18 months [8]. In addition to lowering the risk of stent thrombosis DAPT prevents adverse events consequent to plaque rupture at sites remote from the stented location. According to the authors, this tool needs external validation before recommending its use widely. This tool needs to be used in conjunction with clinical judgment. Our study is extension of the DAPT study. But in our series we found the complication rates were in those patients who had one or two DAPT score.

A meta-analysis by Bulluck and colleagues demonstrated the lack of studies examining a DAPT duration of 12 versus 24 months and showed that although there was no advantage in terms of reducing mortality, MI or stent thrombosis [9]. A prolonged DAPT duration was associated with more bleeding incidents. There was no Asian population in the study. Asian patients may have different profile than western population. Here in our study we have included Asian population only as the study is done in India.

The efficacy of combined antiplatelet therapy was demonstrated in the STARS trial in which patients with aspirin alone had higher cardiovascular complications [10].

Our study showed that, among patients treated with PTCA, there is no reported major bleeding complication. Our results extend the findings from several previous reports which showed a benefit with less death and MI associated with treating patients with DAPT beyond 1 year following DES implantation. A reduction in death was the primary benefit of extended aspirin and clopidogrel [11]. The Duke Registry also found a modest reduction in nonfatal myocardial infarction consistent with the strong trend in our report. Our results reinforce these prior findings and extend them by demonstrating a significant benefit of continued DAPT beyond 2 years following DES placement. Our results are in agreement with findings from the Clopidogrel for the Reduction of Events during Observation (CREDO) trial [12] and the Percutaneous Coronary Intervention-Clopidogrel in Unstable Angina to Prevent Recurrent Events (PCI-CURE) trial which showed a benefit to 1-year of clopidogrel therapy following PCI [13].

LIMITATIONS

There are many limitations to our analysis. First, this is a retrospective and observational registry based study. For example, we did not have data detailing anemia, feature known to be associated with higher mortality. We did not have information delineating the exact time and reason for which the reported complications occurred. We did not make analysis of difference in the complications between first generation and second generation drug eluting stents. Other limitation is that we have not calculated the bleeding risk score along with the DAPT score, to stop or to continue the DAPT.

REFERNCES

1. Mauri L, Kereiakes DJ, Yeh RW, et al. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med. *2014*;371:2155-2166.

2. Colombo A, Chieffo A. Dual antiplatelet therapy after drug-eluting stents—how long to treat [editorial]? N Engl J Med. *2014;* 371:2225-222.

3. Armstrong EJ, Anderson DR, Yeo K-K, et al. Association of dual-antiplatelet therapy with reduced major adverse cardiovascular events in patients with symptomatic peripheral arterial disease. J Vasc Surg. 2015;62(1):157-165.e1

4. Palmerini. Short versus long-term dual antiplatelet therapy after drug-eluting stent implantation: an individual patient data pairwise and network meta-analysis. JACC 2015;65(11):1092-102.

5. Airoldi. Incidence and predictors of drug-eluting stent thrombosis during and after discontinuation of thienopyridine treatment. Circulation. 2007;116(7):745-54.

6. OngA. Thirty-day incidence and six-month clinical outcome of thrombotic stent occlusion after bare-metal, Sirolimus, or paclitaxel stent implantation. J Am Coll Cardiol. 2009; 45:947–953.

7. Ong. Late angiographic stent thrombosis (LAST) events with drug-eluting stents. J Am Coll Cardiol. 2005; 45:2008.

8. Regar E. Incidence of thrombotic stent occlusion during the first three months after Sirolimus-eluting stent implantation in 500 consecutive patients. Am J Cardiol.2004; 93:1271–1275.

9. Iakovou I. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. JAMA.2010; 293:2126–2130.

10. Lagerqvist B, L. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. N Engl J Med. 2007; 356:1009–1019.

11. Eisenstein Clopidogrel use and long-term clinical outcomes after drug-eluting stent antation.JAMA.2007; 297:159–168.

12.Brar SS, Kim J, Brar SK. Long-term outcomes by clopidogrel duration and stent type in a diabetic population with de novo coronary artery lesions. J Am Coll Cardiol.2008; 51:2220–2227.

13. Marroquin OC, Kelsey SF. A comparison of bare-metal and drug-eluting stents for off-label indications. NEngl J Med. 2008; 358:342–352.

14. Shin DH. Reasonable duration of Clopidogrel use after drug-eluting stent implantation in Korean patients. Am J Cardiol.2009; 104:1668–1673.