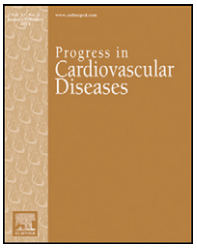
Available online at www.sciencedirect.com

ScienceDirect

www.onlinepcd.com



Duration of Dual Anti-Platelet Therapy Post-Percutaneous Intervention: Is There A Correct Amount of Time?

*Kirk N. Garratt**

Center for Heart and Vascular Health, Christiana Care Health System, Wilmington, DE 19718

ARTICLE INFO

Keywords:
Drug eluting coronary stent
Antiplatelet therapy
In-stent thrombosis

ABSTRACT

Dual antiplatelet therapy (DAPT) is effective in preventing in-stent thrombosis (IST) after placement of drug-eluting coronary stents (DES) and in attenuating risk of athero-thrombotic events, primarily myocardial infarction, among patients with advanced coronary atherosclerosis. However, all studies of DAPT demonstrate an increased risk of moderate or severe bleeding for the duration of therapy. The extent of benefit and risk with various periods of DAPT after DES placement has been evaluated in multiple observational studies and randomized clinical trials. Most studies indicate little or no important reduction of ischemic events but significant increases in bleeding with prolonged treatment. The Dual Antiplatelet Therapy Study was the only randomized trial sufficiently powered to assess IST as an individual endpoint, and this study found that continuing DAPT from 12 to 30 months after DES placement provided important reductions in IST and a composite of adverse ischemic events. When all data are considered, a cogent argument can be made for using just 3 to 6 months DAPT in patients treated with contemporary second generation DES when the goal of treatment is to avoid IST. Longer therapy should be recommended for patients treated with first generation DESs, for whom a persisting signal of IST risk is apparent, and for patients with low risk for bleeding who wish to minimize their risk of athero-thrombotic events, both related and unrelated to DES.

© 2015 Elsevier Inc. All rights reserved.

The dilemma of dual antiplatelet therapy after drug eluting coronary stents

Although drug-eluting stents (DES) have been available for more than a decade, optimal management of patients treated with these products has not been defined. Use of dual oral antiplatelet therapy (DAPT) for a period of at least 12 months following DES placement is recommended currently by the American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI) guidelines[1] and accepted by most (but not all) practitioners in the United States (US), but the ideal period of therapy has not been established. A debate exists about whether the magnitude of ischemic event reduction, especially prevention of in-stent thrombosis (IST), is sufficient to justify the increased bleeding risk associated with prolonged DAPT, and whether or not it is possible to identify those patients most likely to benefit from more intensive antiplate-

Statement of Conflict of Interest: see page 296.

* Address reprint requests to Kirk N. Garratt, MSc, MD, 4755 Ogletown-Stanton Road, Suite 1E50, Newark, DE 19718.
E-mail address: kgarrattmd@gmail.com.

http://dx.doi.org/10.1016/j.pcad.2015.09.001
0033-0620/© 2015 Elsevier Inc. All rights reserved.

Abbreviations and Acronyms

ACS = acute coronary syndrome

ADP = adenosine diphosphate

ARC = Academic Research Consortium

ASA = aspirin

BARC = Bleeding Academic Research Consortium

BMS = bare metal stent

CAD = coronary artery disease

CV = cardiovascular

DAPT = dual anti-platelet therapy

DES = drug-eluting stent

FDA = Federal Drug Administration

IST = in-stent thrombosis

MACCE = major adverse cardiovascular and cerebrovascular events

MI = myocardial infarction

PCI = percutaneous coronary intervention

PES = paclitaxel-eluding stent

RCT = randomixed clinical trial

SCAAR = Sweedish Coronary Angiography and Angioplasty Registry

US = United States

let medications. What is the evidence for and against prolongation of DAPT?

The evolution of DAPT

Antiplatelet medication, chiefly aspirin (ASA), was accepted as useful therapy after placebo-controlled studies in the 1980s and 1990s[2–5] found favorable reductions in composite ischemic event endpoints for ASA, ticlopidine, and clopidogrel. Few physicians considered using two oral antiplatelet drugs together, however. As coronary stent trials progressed from the mid-1980s through the early 1990s, combinations of medications were tested to control IST, an event many felt was inevitable with placement of a metallic device into a diseased coronary artery. Subcutaneous enoxaparin and oral warfarin were intuitively attractive and used widely with limited evidence of effectiveness, either alone or in combination with ASA and other oral antiplatelet therapies. Bleeding rates were high but tolerated because prevention of thrombotic events was considered paramount, and because the period of vulnerability was short: observational reports suggested that antithrombin and/or antiplatelet therapy could be discontinued after as little as 14 days.[6] Several clinical studies were launched to identify an optimal drug program, but a clearly superior therapy had not been determined when the Gianturco–Roubin coronary stents (1993) and Schatz–Palmaz coronary stents (1994) were approved by the US Food and Drug Administration (FDA). In 1998, the Stent Anti-Thrombotic Regimen Study (STARS) confirmed that 30 days of ASA plus ticlopodine was superior to ASA alone and to ASA plus warfarin in preventing IST and achieving low bleeding rates,[7] and dual antiplatelet therapy (DAPT) became the standard of practice. Clopidogrel caused less diarrhea, rash, and idiopathic thrombocytopenic purpura than ticlopidine, and so became the preferred thieopyridine for cardiovascular (CV) uses.

In 2001, the CURE trial proved that the combination of clopidogrel plus ASA was superior to ASA alone in providing protection against recurrent ischemic events in all patients following an acute coronary syndrome (ACS),[8] not just the subset of patients treated with percutaneous coronary intervention (PCI).[9] Serious bleeding occurred in more than 3.5% of patients over 12 months, but this was considered acceptable. A year later, the CREDO trial found similar benefits in patients with stable or unstable symptoms undergoing PCI[10] and DAPT was adopted as standard therapy for most patients with coronary artery disease (CAD).

Two new oral antiplatelet medications have been approved in the past 10 years by the US FDA for use in ACS patients treated with coronary stents: prasugrel is, like clopidogrel, a thienopyridine competitive adenosine diphosphate (ADP) receptor inhibitor. Ticagrelor is a cyclo-pentyl-triazolo-pyridimide compound that acts as an allosteric ADP receptor inhibitor. Both of these agents provide faster onset of action and a higher degree of platelet inhibition than standard doses of clopiodgrel, and have been shown in randomized clinical trials (RCTs) to lower risk of IST compared with clopidogrel, albeit at greater risk of bleeding. Cilostazol and dipyridamole have been used in combination with ASA, but are less potent, less well-studied for IST reduction, and may have somewhat less favorable side-effect profiles. Vorapaxar is a protease-activated receptor antagonist that reduces the ability of activated thrombin to induce platelet activation; limited data suggest that this drug may reduce IST risk when added to standard DAPT, but increases bleeding.[11]

Why do stents clot?

Of many factors believed to contribute to an increased risk of late IST with DESs, most attention focused on (1) the polymers used in first generation stents, which were believed to be insufficiently biocompatible; (2) the drug released, with paclitaxel of particular concern; and (3) structural properties of the stents, such as the thickness of the stent struts. These characteristics were believed to induce significant early injury and thrombosis, and trigger delayed endothelial recovery with persisting inflammation beyond 6 months, based on animal model observations and autopsy studies.[12,13] Second generation stent products were intended to improve late healing and reduce risk by addressing these concerns.

Patient-related factors linked to an increased risk of IST include the presence of cytochrome P450 enzyme alleles that impair clopidogrel metabolism, imperfect stent placement (especially under-expansion), complex coronary artery anatomic characteristics, and certain patient clinical features such as advanced age, hypertension, diabetes mellitus, cigarette smoking, active malignant disease, and presenting with an ACS.[14,15] Risk scoring systems have been developed to aid in estimating risk for individual patients,[16–18] but none of these methods have been validated in populations that were treated with a significant proportion of second generation DESs, so use of these tools for patient risk stratification in a contemporary practice is problematic.

Download English Version:

https://daneshyari.com/en/article/3006280

Download Persian Version:

https://daneshyari.com/article/3006280

Daneshyari.com