

EDITORIAL COMMENT

Noncompliance and Cessation of Dual Antiplatelet Therapy After Coronary Stenting



Looking at the Speck Rather Than Noticing the Log?*

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“Why do you look at the speck that is in your brother’s eye, but do not notice the log that is in your own eye?”

—Matthew 7:3 (1)

A distinctive feature of interventional cardiologists relies in the fact that they take care of patients well before and after the invasive procedures. This explains why the most appropriate medical management following percutaneous coronary intervention (PCI) remains a key issue for interventionalists.

History reminds us that the first stents (Wallstent and Palmaz-Schatz) were plagued by an almost unethically high short-term risk of thrombosis. Antonio Colombo’s breakthrough with dual antiplatelet therapy (DAPT) ushered a new era for stenting, shifting the focus from thrombosis to restenosis. Yet, the advent of drug-eluting stents (DES) more than 10 years ago brought again a wave of uncertainty on the safety of PCI, and in 2006 the European Society of Cardiology Congress highlighted the potentially deadly hazard associated with DES (2).

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This preamble is important to put into context what was decided and recommended by many experts in 2007: routine DAPT for at least 12 months in everybody receiving a DES (3). Indeed, a simple Google Scholar search for “dual antiplatelet therapy discontinuation” shows the 2 most cited articles are this guideline itself and a 4-patient case series (3,4). This is keeping with the lack, until recently, of any randomized trial focusing on this issue.

Some more robust evidence on DAPT has been published recently (5), and further insights will be provided by their synthesis with pairwise and network meta-analyses (6,7). On one hand, the 12-month dogma has been challenged and shorter-term regimens envisioned. Yet, the DAPT (Dual Antiplatelet Therapy) study has highlighted that a 30-month regimen may reduce thrombotic events, albeit at the possible expense of an increase in apparently non-cardiovascular death (5). The scenario on the most appropriate antithrombotic management after coronary stenting is also compounded by the large evidence base suggesting that premature cessation of DAPT is prognostically unfavorable (8,9). There is, however, a problem with terminology because different types of cessation can occur (Table 1).

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This issue of *JACC: Cardiovascular Interventions* provides incremental data with the EDUCATE registry (10). This 2,265-patient prospective observational study focused on nonadherence to DAPT after PCI (originally prescribed for 12 months). Nonadherence was defined as missing ≥ 1 day of DAPT, whereas severe nonadherence was defined as missing ≥ 2 weeks. After 6 months, nonadherence occurred in 9.6%

TABLE 1 Type, Subtype, Incidence, and Consequence of Suboptimal DAPT After Coronary Stenting

Type	Subtype	Definition	Incidence	Prognostic Impact
Underuse	Not established	Act of using (or prescribing) less than expected	+	+
Noncompliance	Not established	Inaccuracy with which a patient follows an agreed treatment plan	+	+
Cessation	Interruption	Physician-supervised temporary cessation	++	+/-
	Discontinuation	Physician-supervised permanent cessation	++	+/-
	Disruption	Cessation due to noncompliance or actual bleeding	+	++

++ = high/strong; + = moderate; +/- = low/mild; DAPT = dual antiplatelet therapy.

and severe nonadherence in 5.2%, and the only independent predictor of nonadherence was major bleeding. Nonadherence up to 6 months was associated, even at multivariable analysis, with an increased 12-month risk of death/myocardial infarction (odds ratio: 1.95 [95% confidence interval: 1.02 to 3.75], $p = 0.045$). Notably, nonadherence up to 3 months or between 3 and 6 months were similarly detrimental, whereas nonadherence after 6 months did not appear impactful.

What are the key strengths of this work? First, the relatively large size and ensuing statistical precision. Second, the prospective design and reliance on a single DES, thus increasing precision. Third, the participation of institutions with state-of-the-art facilities and expertise.

Yet, some drawbacks may be highlighted. First, there is no detailed analysis on the type and subtype of nonadherence. In particular, it has been shown that disruption is the most ominous variant of nonadherence, whereas other subtypes are more benign (9). Second, this work misses the opportunity to unify

the many elements underpinning decision making on DAPT by simultaneously and appropriately weighing benefits and risks. Third, the focus on phosphoryl-coated zotarolimus-eluting stents partly undermines the importance of the report because this stent is considered rather obsolete in many settings, given its suboptimal antirestenotic effect (11). Fourth, lumping together short-term nonadherence and longer episodes of nonadherence appears superficial, because brief cessations may be rather safe (8,12). Fifth, the large confidence intervals and the marginally significant p value do not prove strictly convincing and could hint at residual confounding. Sixth, the focus on a 6-month threshold has been already challenged, especially when using DES with a superior safety profile (6). Seventh, there was no chance in this study to test or appraise means to minimize noncompliance or cessation. Although some approaches (such as the Interactive Monitoring Service, FBCommunication, Modena, Italy) have been advocated, the evidence base on them is still scant, and even observational perspectives could be useful.

In conclusion, underuse, noncompliance, and cessation of evidence-based antithrombotic therapies remain important and potentially hazardous for patients undergoing PCI with DES. More focus is, however, needed also on the subtleties of this clinical conundrum, including treatment individualization for drug type, dosage, duration, and combination. Otherwise, we may risk unduly looking at the speck rather than at the log of safe, effective, appropriate, and affordable cardiovascular care.

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