

Summary Statement on Late and Very Late DES Thrombosis.

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Early stent thrombosis occurs in about 1.0% of patients who receive either drug-eluting (DES) or bare metal (BMS) stents. However, both late and very late DES thromboses have recently been recognized as a potential complication of DES deployment. Enormous attention has been paid (in both the medical literature and lay press), to this potential adverse event following DES due to the associated high morbidity and mortality. As often occurs with medical reporting in mass media, the public has been presented with mixed messages comprised largely of sound bites rather than the full information readers need to discern the truth. For physicians, the accurate assessment of risk for stent thrombosis related to DES has been difficult for several reasons. First, the definition of what constitutes stent thrombosis has been the subject of debate. Second, this dreaded event occurs infrequently and thus, requires analysis of several thousand patients followed for well beyond one-year duration to detect. Third, randomized controlled trials which have adhered to relatively narrow participation criteria and have excluded more complex “real world” patients may under-represent the true magnitude of this problem. Fourth, “very late” stent thrombosis events must be differentiated from the 1 to 2% yearly “background” incidence of death or myocardial infarction observed in patients with CAD which is attributable to plaque rupture or progression in non-stented coronary segments. Finally, we now appreciate that late (beyond 1 year) stent thrombosis did occur following BMS deployment (albeit rarely), particularly if all antiplatelet therapy (including aspirin) was discontinued.

As you know, the FDA panel met on December 7th & 8th, 2006, to discuss and analyze recent data concerning late DES thrombosis. After reviewing all available data from industry and following an open public session, the panel has provided the following summary:

1. DES, when used in accordance with their FDA approved and labeled indications, are associated with a numerical excess of late stent thromboses (after 1 year implantation) compared to BMS; however the magnitude of this excess is uncertain and additional data are needed.
2. DES are not associated with an increased risk of death or myocardial infarction (MI) compared to BMS.
3. DES are not associated with an increased rate of all-cause mortality, but longer-term follow-up and an increased number of patients in future trials was requested.
4. Safety concerns apply equally to both currently approved DES, but do not outweigh their benefits compared to BMS when used according to approved labeling.
5. Antiplatelet therapy following DES implantation should follow the current ACC/AHA/ SCAI clinical practice guidelines for percutaneous coronary intervention (12 months of aspirin and clopidogrel therapy for patients at low risk for bleeding complications).

6. The off-label use of DES, like bare metal stents, is associated with increased risk compared with on-label use. Available data were insufficient to identify specific subsets of patients at particularly increased risk for stent thrombosis.
7. There was agreement that the data for off-label use are limited and the panel recommended larger and longer follow-up for post-approval studies, with specific and uniform definitions for stent thrombosis events.
8. The panel also agreed that at least 12 months of dual antiplatelet therapy should be recommended following off-label DES use.

Ongoing data collection from large registries, as well as planned clinical trials with stent thrombosis as the primary endpoint, will provide further information how to best utilize this technology in the treatment of our patients with CAD.

REFERENCES:

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