
To the Editor:

Randomized controlled clinical trials of drug-eluting stents (DES) versus bare metal stents demonstrate no differences in the cumulative 4-year incidences of death or myocardial infarction using the Academic Research Consortium definitions. Nevertheless, a numeric increase in the incidence of late stent thrombosis (LST) after DES implantation has been observed. LST attributable to DES may be explained by (1) a relationship to the antirestenotic properties of DES (reduced late lumen loss), (2) the impact of drug and polymer components on thrombosis, (3) the propensity to treat patients previously not treated with bare metal stents because of high restenosis risk, and (4) newly recognized limitations of standard antiplatelet therapies that may increase the risk of LST.

Camenzind et al have proposed a relationship between lumen loss in-stent as measured by quantitative coronary angiography and LST by postulating positive remodeling accompanied by diminished or absent endothelial coverage and stent healing. Apparent support for this mechanism is derived from a cartoon (Figure 2) that depicts the speculative pathophysiological relationship between low or negative values for late lumen loss and LST. Unfortunately, this curve is not based on actual data. These authors represent late lumen loss in-stent after DES with a Gaussian curve in which similar portions of measurements reside both above and below the mean value for a specific device. However, the distribution curves for late lumen loss after DES implantation do not follow a normal distribution but instead become progressively rightward skewed at lower levels of late loss approaching zero. Furthermore, such a high incidence (~50%) of negative late loss has not been observed in most of the large angiographic studies involving first-generation DES, and such a high rate of positive remodeling has not been reported from intravascular ultrasound substudies. Calculations of negative late loss likely represent the known errors in quantitative measurement from serial angiograms in which the measurement error exceeds the mean value for late loss rather than a systematic gain in lumen diameter after DES. Finally, Camenzind et al fail to acknowledge the conceptual and likely real differences between neointimal proliferative response, mechanical endothelial coverage, and optimal healing, which would entail coverage with mature, normally functioning endothelium.

The extrapolation from late lumen loss in-stent (neointimal tissue in-growth) to the separate and potentially distinct process of healing and endothelial coverage is neither appropriate nor supported by data. We believe that LST after DES implantation has several potential pathogenetic mechanisms, including delayed/incomplete endothelialization and healing, polymer-related hypersensitivity/inflammation, late acquired incomplete stent apposition, and compliance with and/or resistance to combination (aspirin and thienopyridine) antiplatelet therapy. The serious problem of LST requires further investigation of causes and estimation of rates and is not explained primarily by positive remodeling, as suggested by Camenzind et al.

Disclosures

None.

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