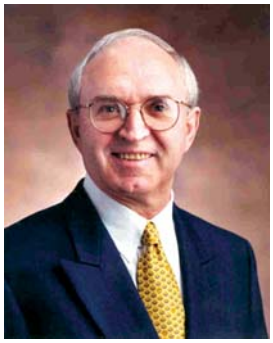
President's Page

Drug-Eluting Stents: A State of Uncertainty



HARISIOS BOUDOULAS, MD, PhD

Foundation of Biomedical Research, Academy of Athens, Greece

"I know nothing except the fact of my ignorance." Socrates

Angioplasty with stent placement is a well established method for the treatment of patients with obstructive symptomatic coronary artery disease. However, the incidence of restenosis with first generation bare-metal stents is high. For this reason, drug-eluting stents were introduced into clinical practice. These stents have substantially decreased the incidence of early restenosis and have thus resulted in a significant reduction in the need for repeat revascularization. It is not surprising, therefore, that drug-eluting stents have been used widely worldwide since their introduction in 2003. It is estimated that approximately six million patients have been treated with drug-eluting stents.

Recent data, however, have suggested that there is a small increase in the rate of death and myocardial infarction, probably due to late stent thrombosis, in patients who have received these stents. Although the incidence of late thrombosis is not exactly known, it is estimated to be 0.2 to 0.5% per year. Also of concern is the fact that late stent thrombosis has been observed as long as eighteen months to three years after implantation. To avoid stent thrombosis, dual antiplatelet therapy with clopidogrel and aspirin is recommended. Initially, it was suggested that this therapy should be continued for three to six months, depending on which type of drug-eluting stent the patient received. Recent data, however, indicated that there is a greater risk for thrombosis if therapy with clopidogrel was discontinued even twelve months after stent placement. Given that more than one million patients receive drug-eluting stents each year, even a small increase in the risk of late thrombosis could result in thousands of myocardial infarctions and deaths.

Because of the great importance of the problem, the Food and Drug Administration (FDA) met earlier this year with manufacturers of these stents in order to discuss further the available information related to late stent thrombosis. The FDA will also meet with a panel of experts on December 7 and 8 in an effort to improve current knowledge regarding the incidence and timing of thrombosis of drug-eluting stents.

Uncertainties related to drug-eluting stents

The risk of late stent thrombosis appears to be real, but its magnitude is in question. It is unclear what causes stent thrombosis, under what circumstances it occurs, or what the risk of occurrence is in a given patient. It is not known whether certain patients are prone to thrombosis (e.g. platelet polymorphism of glycoprotein IIβ-IIIα). Likewise, the optimal time (if any) to discontinue the antiplatelet therapy is not known. Long term dual antiplatelet therapy is associated with risks of bleeding, especially in patients who will need surgical procedures. Thus, it is often difficult to make a rational decision on what to do with the patient who already has a drug-eluting stent or with a patient who needs a stent. To solve these problems we obviously need more data.

Despite these uncertainties, and until the results of future studies become available, as physicians we have to take action for the individual patient we are treating. The physician must be aware of his/her limitations, but should also realize that he/she often has to make important decisions related to patients' care without having complete information. It should be emphasized that the physician must have the ability to

perform in an atmosphere of uncertainty. Our decisions must be based on knowledge, experience and most importantly, on common sense.[1,2] Drug-eluting stents should be used based on current indications, but their use should not be expanded beyond these indications. We should also be aware that these indications are in constant evolution. It is of equal or even greater importance that therapy with drug-eluting stents should not be denied to patients because of the fear of late stent thrombosis. Dual antiplatelet therapy in patients with drug-eluting stents should be continued at least for twelve months and in certain cases indefinitely. It should be emphasized to patients who have drug-eluting stents not to discontinue therapy with clopidogrel and aspirin, because this could be life threatening. As physicians, we should comfort the anxious patient with drug-eluting stents who worries about thrombosis. Finally, despite these problems and uncertainties, available information at present suggests that the benefits of drug-eluting stents far outweigh the risks.

References

1. Peabody FW: The care of the patient. JAMA 1984; 252: 813-818.
2. Boudoulas H: The well-rounded clinician. Hellenic J Cardiol 2005; 46: 317.