Point/Counterpoint

Is it time to scale back the use of drug-eluting stents?

Bare-metal stents are underused.

Given the recent signals of an increased risk of late thrombosis with drug-eluting coronary stents, cardiologists should be cautious and use more bare-metal stents for percutaneous coronary interventions. Special caution should apply to patients who are unlikely to be able to adhere to a clopidogrel regimen because of the drug's cost, pending surgery, or other reasons, and for patients who need stenting of large arteries that have a relatively low risk of restenosis.

Routine use of drug-eluting stents is also questionable in patients who need stents in complex lesions that don't have a labeled indication for a DES, because it's these cases that seem to pose the biggest risk for stent thrombosis.

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Because the data behind these signals are too limited to be clear-cut proof, considerable uncertainty remains about the exact danger posed by drug-eluting stents and the correct role today for these devices. Also unclear is the best way to manage patients with a coronary DES in place. Although indefinite continuation of dual antiplatelet therapy seems the best way to reduce future risk for stent thrombosis, patients also face a bleeding risk with ongoing treatment with clopidogrel and aspirin.

If patients with a DES have just a 0.5% excess risk of death or major myocardial infarction each year after their first 6-9 months of follow-up, which is what recent findings suggest, then the 15-year life expectancy of patients with a coronary DES will be limited by a major, cumulative risk for adverse outcomes that could potentially affect hundreds of thousands of patients. This risk seems linked to two main problems with the stents now on the market: a failure of the vascular endothelium surrounding the stent to heal quickly and a hypersensitivity reaction to the stent coating.

Signals of a problem emerged from three reports issued last year. Results from the Basel Stent Kosten Effektivitäts Trial—Late Thrombotic Events (BASKET-LATE), first reported at the annual meeting of the American College of Cardiology in March 2006, showed that in 499 patients who received a DES, the risk of death or myocardial infarction during 7-18 months after implantation was 4.9%, compared with a 1.3% rate in 244 patients who received a bare-metal stent, a statistically significant difference.

This trial was followed by two reports from the joint meeting of the European Society of Cardiology and the World Heart Federation in September 2006. Both of these overviews combined longer-term follow-up results from the pivotal trials of the two types of drug-eluting stents that are on the U.S. market. One overview of 17 trials found an excess of deaths with drug-eluting stents, especially in noncardiac mortality. I don't know why this might have occurred, but the magnitude of the difference seemed to increase with time.

In addition, a DES registry report at the scientific sessions of the American Heart Association in November 2006 found that by 6 months after stent placement, the majority of stent thromboses, myocardial infarctions, and cardiac deaths occurred in patients who received a DES for an off-label use.

The trials that led to approval of drug-eluting stents enrolled only relatively low-risk patients with simple lesions. But recent registry data show that most patients get a DES for more challenging, off-label lesions. In the easy cases that made up the trials, overall event rates were low, which meant a reduced power to detect differences between drug-eluting and bare-metal stents in these low-frequency events.

We're in a period of great uncertainty about the ongoing risk to patients who get a DES for an off-label indication. It seems that these stents are best reserved for perhaps half of all stenting cases. Bare-metal stents should be favored in patients who face surgery in the next 3 months and in patients who don't have reliable access to clopidogrel such as uninsured patients. ■

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Drug-eluting stents are the standard of care.

Drug-eluting coronary stents are unquestionably the standard of care for percutaneous coronary interventions in most patients because they reduce the frequency of restenosis by approximately 70%, compared with bare-metal stents.

Although recently reported data have generated hype and hysteria about the potential for increased rates of death and myocardial infarctions with drug-eluting stents, a more careful analysis of the data from randomized clinical trials shows no evidence that DES cause a higher overall frequency of death and MI, compared with bare-metal stents. Drug-eluting stents do appear to be associated with a slightly higher frequency of very late stent thrombosis (about 0.5%). However, this is balanced by the decrease in death and MI associated with the reduction in the rate of restenosis.

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Importantly, the risk of late thrombosis is real and should be addressed by careful patient counseling regarding medication compliance and prolongation of dual antiplatelet therapy following DES placement. We have also begun to recommend "less aggressive" use of drug-eluting stents overall, such as avoiding the use of two drug-eluting stents when treating stenoses at a coronary bifurcation. Undoubtedly, bare-metal stents (BMS) are a better option for patients who face problems continuing dual antiplatelet therapy with clopidogrel and aspirin for a prolonged period of time.

A major factor supporting use of drug-eluting stents is that restenosis does not have a benign outcome following percutaneous coronary intervention. Results from two independent studies reported last year showed that about 10% of patients who develop restenosis following placement of a BMS have an acute MI as their first manifestation. In one report involving almost 1,200 patients who had instent restenosis following placement of a BMS, the acute mortality after restenosis was 0.7%.

The reports of increased late thrombosis with drug-eluting stents that produced the recent concerns excluded events that occurred after a repeat intervention due to restenosis. Because there is a much higher frequency of restenosis after the use of a BMS, many of the thrombosis episodes after restenosis were not counted. New definitions of stent thrombosis have been proposed by the Academic Research Consortium and after careful, independent adjudication of all events employing these revised definitions, there were no overall differences in stent thrombosis between the DES and the BMS.

Nevertheless, concerns about drug-eluting stents have led to a plateau and then more recently a decline in their use. Last year, DES use in the United States had fallen about 20% to a level of approximately 70%-75% of all stent procedures. In Europe, the overall use of these stents is approximately 50% of all stent cases.

We are now counseling patients who have a DES to remain on clopidogrel and aspirin for at least 1 year, and longer in some cases. We are uncertain if the increased risk of late thrombosis represents a continuous hazard, but our impression is that the event rates have flattened after the first 2 years.

Unfortunately, the predictors of late DES thrombosis are poorly defined and there has been no good link between lesion complexity and the risk of late thrombosis. There is a suggestion that late DES thrombosis may be further increased in so-called off-label use, but these registry data are poorly validated and follow-up has been incomplete.

Despite this new finding of late DES thrombosis, the overall advantages associated with reduction in restenosis still outweigh the risks. Careful patient counseling, prolonged use of dual antiplatelet therapy, and more judicious use of the stents should optimally manage the current situation. Safer drug-eluting stents are being developed that should further restore confidence that this important biotechnology platform is the standard of care for the treatment of obstructive coronary disease. ■

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Intervention Cut Central Catheter–Related Infections in ICUs by 66%

A "simple and inexpensive" intervention to reduce ICU infections related to central catheter lines decreased the infection rate by 66% in 107 hospitals throughout Michigan, according to a new study.

The overall median rate of central catheter–related bloodstream infections was held to zero throughout 18 months of follow-up, said Dr. Peter Pronovost of Johns Hopkins University, Baltimore, and his associates (N. Engl. J. Med. 2006;355:2725-32).

The intervention, part of a statewide program to improve patient safety, targeted clinicians' use of five procedures identified by the Centers for Disease Control and Prevention as having the greatest potential to reduce infection and the greatest ease of implementation. The procedures are appropriate hand washing, using full-barrier precautions during the insertion of central venous catheters, cleaning the skin with chlorhexidine, avoiding the femoral site for access if possible and removing unnecessary catheters.

A hospital-based practitioner was designated as the infection-control specialist. Clinicians were taught infection-control practices, provided with a central-line cart with necessary supplies, given a checklist to ensure adherence to infection-control practices, and stopped if they weren't following the checklist. Catheter removal was discussed every day at rounds, and ICU teams received feedback on infection rates at monthly and quarterly meetings.

This intervention was assessed at 67 Michigan hospitals of all types, which included 103 medical, surgical, cardiac, neurologic, and trauma ICUs and 1 pediatric ICU. Within 3 months of implementation, the overall median rate of central catheter–related bloodstream infection dropped from 2.7 per 1,000 catheter-days at baseline to 0. The corresponding average rates of infection were 7.7 and 2.3, respectively, Dr. Pronovost and his associates said.

—Mary Ann Moon