Drug-eluting stents, long-term safety and the importance of healthy healing

Since their introduction in 2003, drug-eluting stents have become a standard of care for coronary artery disease—the narrowing and hardening of the small arteries that supply blood to the heart. If left untreated, coronary artery disease can cause angina, shortness of breath, congestive heart failure, heart attack and death.

A stent is a tiny mesh cylinder used during angioplasty—a minimally-invasive procedure used to reopen coronary arteries by inflating a tiny balloon in the vessel at the site of the blockage. The stent is crimped tightly around the balloon so that it expands into the walls of the blocked artery as the balloon is inflated. Once the blockage is cleared, the balloon is deflated and removed. The stent, however, remains in place, providing a scaffold to keep the artery open.

Even with a metal scaffold to hold the vessel open, some arteries still become blocked again relatively quickly. This is caused by the growth of too much new tissue inside the vessel as the artery wall heals after the procedure. To limit this new tissue growth and to reduce the likelihood of the artery becoming blocked again, drug-eluting stents were developed. These stents are coated with a drug that elutes from the surface, slowing tissue growth so that the reopened artery remains open. Drug-eluting stents have proved very effective at preventing this tissue growth, perhaps too effective in some cases.

HEALTHY HEALING

Healing inevitably involves the growth of new tissue. Allowing some healing to take place after a stenting procedure enables the re-creation of a functional endothelium (the inner surface of the artery wall). During this healing process, the structure of the stent becomes enveloped in new tissue, creating a biological shield between the stent and the bloodstream. If healing is prevented too effectively, the re-creation of a healthy endothelium is limited, leaving stent struts exposed to the bloodstream. These factors are important as the body is extremely good at identifying foreign objects; in the bloodstream, this can result in the formation of clots. The body also reacts with inflammation when foreign matter is detected; inflammation can also prevent effective healing.

THROMBOSIS

Under normal circumstances, inflammation and the formation of blood clots (thrombosis) are part of an essential, life-saving process. However, in an artery, particularly a small artery supplying a vital organ like the heart, a blood clot can be lethal. Heart attacks and strokes result from the formation of clots that have blocked the flow of blood to a section of heart muscle or to the brain.

It is important for safety to minimize the potential of any component of the stent to cause inflammation or thrombosis. In recent months this has become a significant issue because stent thrombosis (the formation of clots at the site of the stent) has been reported, unexpectedly, many weeks after implantation of both of the first-generation drug-eluting stents available in the US. Although rare, this very late stent thrombosis is unpredictable, potentially fatal and has been occurring long after the healing process should have stabilized the endothelium, covered the stent in new tissue and eliminated inflammation.
Drug-eluting stents, long-term safety and the importance of healthy healing (continued)

THE NEXT GENERATION

If a drug-eluting stent is insufficiently effective at limiting new tissue growth, then the artery will close again. A fine line has to be found, where new tissue growth is limited without preventing healthy healing. A drug-eluting stent with these characteristics would be as effective as the existing drug-eluting stents on the market but would have a safety profile more commonly associated with bare-metal stents, which do not limit the healing process at all. The next generation of drug eluting stents will need to demonstrate these characteristics.

*The graphic below is illustrative of the healthy healing process with the Endeavor drug eluting stent.*