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REDUCING THE RISKS OF STENTS

Doctors should use new devices and procedures to insert drug-eluting stents in order to cut the already low rate of ensuing, fatal blood clots

Tiny mesh tubes called stents have been on a high-stakes medical rollercoaster ride. Starting in 1994, doctors began inserting the metal tubes in the clogged arteries of patients to prop them open. The problem, though, was that those blood vessels closed up again within a few years in up to 30% of recipients, when cells in the vessel walls proliferated and narrowed the arteries. So companies like Boston Scientific (BSX) and Johnson & Johnson (JNJ) developed stents that contain a drug to slow the growth of cells. These so-called drug-eluting stents hit the market in 2003 and took off like a rocket. Sales hit \$6 billion per year in 2006, with about 1 million patients receiving such stents.

But these drug-coated devices began to cause a different, more dangerous problem. The drugs did their work too well. By inhibiting cell growth, they prevented the initial wound in the blood vessel from healing. The result: an alarming rise in cases of serious, often fatal, blood clots. The relative numbers are small: less than 1% of patients. But death is a pretty serious side-effect, and the press began to speculate about these stents being ticking time bombs in patients' bodies. The concern led to a

decline in the use of drug-eluting stents. The devices took another hit earlier this year during a trial questioning the benefits of stents in general. As a result, sales of drug-eluting stents have dropped, (BusinessWeek, 10/29/07) to an expected \$4.1 billion in 2007.

Now, while concerns remain, the scary headlines are beginning to look overblown. The latest data, discussed at this week's annual transcatheter cardiovascular therapies meeting (BusinessWeek, 10/23/06) show that the drug-eluting stents do seem to offer significant benefits, while the rate of fatal blood clots can be very low. But the reassuring news comes with one important caveat: Doctors must do a better job of implanting them. "Because of their promise, there was a lot of misuse," says Dr. Georgios Sianos, senior interventionalist at the Erasmus Medical Center, Rotterdam, Netherlands. Thinking that the devices were like a magic bullet, doctors often didn't insert them carefully enough, Sianos says.

USING ANGIOJET TO SUCK OUT THE CLOT

To understand one reason why, picture a blood vessel that is becoming

diseased. Bits of cells and clotting factors can stick to the side of the vessel, creating a clot. The accumulating crud can block the artery, causing a heart attack, or just narrow it, causing symptoms like angina. To treat the problem, doctors thread a catheter through the blood vessels up to the narrowed point. The physicians then expand a balloon at the tip of the catheter, opening up the artery. The balloon also expands a stent until it is wide enough to neatly fit the newly opened vessel and hold it open.

In walls coated with crud, however, doctors face a dilemma. They can force open the stent so that it pushes hard into the clotted material. But some of the clot might break off and cause a heart attack. Alternatively, they can leave the stent more gently touching the layer of clot. The second approach can lead to more heart attacks months or years later. The reason: After the clot is gradually dissolved away by drug treatment, a gap appears between the stent and the vessel wall. The too-small stent then can't do a proper job of keeping the vessel open. And the gap becomes a potential site for dangerous new clots to form.

The solution? From his results in Rotterdam, Dr. Sianos believes that answer lies in an additional step before inserting the stent. His team uses a device created by Minneapolis-based Possis Medical (POSS) to remove the clot, or thrombus, first. Called AngioJet, the device employs a stream of water to remove and suck out the clot. "The bottom line is that when you take the thrombus out, patients do significantly better," says Sianos. In the patients who arrive at the hospital with big clots, the risk of later heart attacks is cut as much as ninefold if the clots are removed before the stents are inserted.

USING THE SHORTEST POSSIBLE STENT

Doctors figure that about 10% of all

patients having stents, or about 100,000 patients a year, would benefit from clot removal. If the procedure does catch on, that would mean up to a \$170 million per year market for Possis' \$1,700 clot-busting procedure. "It is pretty exciting for us," says Possis President and Chief Executive Robert G. Dutcher.

Clot removal is just one example of how doctors can use stents better. Another key is using the shortest possible stent to correct a narrowing, since the risk of later heart attacks goes up as the stents get longer. And the stents themselves are being improved. In some of the initial drug-coated devices, the drugs stay around too long, inhibiting healing of the original wound too much. Newer versions

release all of the drug sooner, and one experimental version even dissolves away completely.

There still is a debate raging about whether most patients need stents at all, since drug treatment and lifestyle changes can be as effective. And doctors who are in the business of inserting stents have a professional and financial interest in continuing to use them. But as they learn to use the devices more effectively, and employ better devices, chances are that stents will remain a big business.

By John Carey

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