Trends-in-Medicine

July 2006

by Lynne Peterson and D. Woods

Quick Pulse

Trends-in-Medicine
Stephen Snyder, Publisher
2731 N.E. Pinecrest Lakes Blvd.
Jensen Beach, FL 34957
772-334-7409 Fax 772-334-0856
www.trends-in-medicine.com

STENT UPDATE

In the U.S., use of bare metal stents (BMS) is ***not*** increasing at the expense of drug-eluting stents (DES). That's the consensus of DES manufacturers as well as interventional cardiologists and cardiac cath lab managers.

On June 22, 2006, the ***Wall Street Journal*** reported that "rising concern over potentially deadly blood clots has led some cardiac centers to cut back on use of drug-coated stents." The ***Wall Street Journal*** admitted that "hospitals aren't drastically curbing use" of drug-eluting stents and noted that "there's no indication yet of an overall decline in (DES) sales," but five of the six cath labs mentioned in the story had cut their drug-eluting stent use, which might suggest that this is a trend.

***Wall Street Journal*: Cath Lab DES Use Changes**

Cath lab	DES use
Washington Hospital Center, Washington, DC	Down 5% vs. 6 months ago
Cedars Sinai Medical Center, Los Angeles, CA	Down 7% (from 93% to 86%) in the first 4 months of 2006 vs. the last half of 2005
Brigham & Women's Hospital, Boston, MA	Down "a small but significant" amount
Cleveland Clinic, Cleveland, OH	Down 3%-4% over the past 6 months
University of Chicago, Chicago, IL	Down 5%-10% (from 90% to 80%-85%) compared to two years ago
William Beaumont Hospital, Royal Oaks, MI	Flat but may increase in the near future

However, a check of 18 other cardiac cath labs – half medium-to-large community hospitals and half academic medical centers – found that use is flat compared to six months ago, and the outlook is for usage to remain flat for the next 6-12 months. This larger sample did not confirm the ***Wall Street Journal*** findings.

On average, cath lab managers estimated that drug-eluting stents account for 91% of all stents used in their labs. Among these sources, usage over the past six months has been:

- **Flat** for 14. "There has been no change in our drug-eluting stent use" was the repeated comment. A Midwest cath lab manager said they saw a little drop in DES use – but not recently, "At first everyone got a drug-eluting stent. But our change – putting in a few more bare metal stents in larger (3.5 mm) vessels – occurred ***last year***."
- **Up slightly** for 4. An East Coast manager said, "Our DES use is actually up

3%-4%. The only time we use a bare metal stent is if we don't have the right size drug-eluting stent." Another commented, "Our DES use is increasing." The director of a cath lab that was affected by Hurricane Katrina last year said, "Our overall, absolute DES usage is up compared to a year ago and up slightly over the past six months as our cath lab volume has increased…As early as six months ago, we had recovered much of our pre-Katrina volume. Our lab has had an aggressive approach to PCI (percutaneous intervention), and I believe that 6-12 months ago we had already incorporated the impact of DES into our decision-making with respect to PCI."

Bare metal stent usage

Indeed, most interventional cardiologists and cath lab managers were emphatic that BMS are only used where drug-eluting stents are contraindicated or unavailable.

- *New York:* "We are still using drug-eluting stents in most patients, the major exceptions being patients considered for non-cardiac surgery or with 4.0 mm vessels."
- *Arkansas:* "Our doctors are behind drug-eluting stents 200%...We have had a huge decrease in restenosis (with DES)…We don't consider anything but drug-eluting stents…We only use bare metal stents in larger vessels (4.0 mm), where no DES are available."
- *Florida:* "We are using bare metal stents for large (4.0 mm) and small (2.0 mm) vessels. Recent data suggest that when you have someone with an acute MI, you are somewhat safer using a BMS rather than a DES due to stent thrombosis. How much validity that study has, I don't know. It has influenced a couple of physicians, but most are still using DES in the setting of AMI (acute myocardial infarction)."
- *Kansas:* "The only time we use a BMS is (1) if we have patients who come in presenting acutely and really need surgery, but we need to fix something to get them to surgery, (2) if there is a question about patient follow-through on Plavix (Sanofi-Aventis, clopidogrel), or (3) if we don't have the DES size. DES are limited to 2.5-3.5 mm x 33 mm (with Johnson & Johnson's Cypher). Beyond that, we have to go to a BMS."
- *Louisiana:* "We employ bare metal stents for patients in whom a drug-eluting stent cannot be implanted for technical reasons, such as trackability. The risk of restenosis for people with diabetes is increased 10% in actual (not relative) risk. Diabetics are more likely to benefit from DES. We do not discriminate against the elderly. There are no DES designed for vessels >3.5 mm, so those patients are more likely to get a BMS. Patients who are unable to take prolonged dual antiplatelet therapy and those in whom we anticipate surgery which cannot be deferred are more likely to have a BMS."
- *Indiana:* "We've always been somewhat conservative. We use bare metal stents for acute MI and in patients where we're worried about compliance with Plavix. We also use a bare metal stent if the patient has an unexplained anemia or needs upcoming surgery. We use drug-eluting stents for sure in diabetics, longer lesions, bifurcations, left mains, and small vessels. Vein grafts are a tossup."
- *Illinois:* "In terms of evidence-based medicine, it is obvious the restenosis rate is much better with DES than BMS, so any coronary artery 3.5 mm and below should receive a DES. For vessels 3.75 mm and above, there is no statistically significant difference in restenosis rates between DES and BMS, so above 3.5 mm there is no advantage to drug-eluting stents, and they are a lot more expensive."
- *California:* "The most common reason for not implanting (a DES) is the patient's inability to take prolonged clopidogrel in combination with aspirin."

Yet, cardiologists appear to be more comfortable using a bare metal stent today than they were 6-12 months ago. A Midwest cardiologist explained, "Our use of DES is flat, but our threshold for using bare metal stents has gone down. If someone comes in with an acute MI (AMI), we are probably just as likely to use a BMS as a DES. As a teaching hospital, we take care of a lot of indigent patients, and the ability of indigent patients to be on long-term Plavix is a real issue. So, for those patients, I am more likely to put in a BMS…People don't die of restenosis, but they do die of stent thrombosis. I don't think they (indigent patients) understand the implications of not taking their Plavix."

Outlook for next 6-12 months

For the next 6-12 months, most sources predicted that drug-eluting stent usage would be flat compared to current levels. A Louisiana doctor said, "Barring new data, I anticipate our mix of DES and BMS to be flat…and I expect that our total orders will continue at current levels." A Midwest doctor said, "For the next 6-12 months, our use of DES will be flat, but over the next 2-5 years, use of DES will continue to creep upward because second- and third-generation DES are coming, and DES are becoming more deliverable." A California cardiologist said, "I think some groups who embraced DES for 100% of patients will back off a bit." A Midwest cardiologist said, "I think our DES number will be stable or increase slightly over the next six months, unless there is more information that late stent thrombosis is a bigger problem than we believe it to be."

Even Dr. Ron Waksman at the Washington Hospital Center, who was cited in the ***Wall Street Journal*** article, doesn't expect his cath lab's drop in DES use earlier this year to continue, "I think usage will be flat over the next six months. I don't think the numbers will continue to fall unless there is more bad news from the DES front." He explained why DES usage fell 5% this year at his hospital: "The reason is sub-

acute thrombosis and late thrombosis. This is not exclusive only to Washington Hospital Center, but it is not affecting all (cath) labs. Some still use DES for all patients. We stopped treating AMI with DES and switched to BMS for large vessels and focal lesions. This is not across all physicians…The statement by Dr. Rob Califf (Duke University) that DES is a life sentence to Plavix also has to do with that."

While drug-eluting stents are being used for expanded and off-label indications, such as bifurcations and in-stent restenosis, sources said these uses are not significantly boosting overall DES use.

Stent thrombosis

Doctors and cath lab managers are worried about stent thrombosis, but for most this has translated into more aggressive use of Plavix longer and/or emphasizing to patients the importance of taking the prescribed Plavix.

- *Arkansas cath lab manager:* "We've seen a couple of SATs (subacute stent thromboses), and it is often enough to be a concern, but usually it happened when patients stopped taking their Plavix. We keep patients on Plavix at least a year."
- *New York cardiologist:* "There is increasing concern about very late stent thrombosis occurring in some patients more than a year after implantation, but this phenomenon remains quite infrequent and has not changed our practice."
- *Midwest cath lab manager:* "If patients don't follow through with their Plavix, that significantly raises the bar for stent thrombosis, but if they take their medicine like they are supposed to, we just don't see that happen. We've had some SATs, but guess what – they quit taking their Plavix! 'Hmmm, did you not understand what we told you?' We tell them, 'I don't care what another doctor or pharmacist tells you, you do ***not*** stop this (Plavix) unless our cardiologist tells you to.'"
- *New Jersey cath lab manager:* "We really have no SATs here. We really follow with Plavix. In fact, if a patient goes to another service in our hospital within the next year, it is noted in the patient's medical records to contact us before stopping Plavix."
- *California cardiologist:* "Stent thrombosis is the issue. Cost – of the clopidogrel, not the DES – is an issue. To the extent that drug-eluting stents have a higher incidence of stent thrombosis, you have traded a relatively benign (albeit costly and inconvenient for the patient) condition – restenosis – for a rare but much more lethal (30% mortality) condition, stent thrombosis. There is no subgroup in whom drug-eluting stents are not superior in terms of restenosis, but the magnitude of the effect is less in non-diabetics, larger vessels, and shorter lesions."
- *Midwest cardiologist:* "The concern about stent thrombosis is the No. 1 issue with drug-eluting stents. I don't think people are as worried about restenosis...Stent thrombosis is a killer; restenosis is an inconvenience… The current atmosphere may be ripe for the Medtronic Endeavor platform – a 'DES-lite' with good safety."
- *Another Midwest cardiologist:* "When there is a new coronary device – and DES are still in that classification – interventional cardiologists embrace them with unrealistic enthusiasm…They like new devices and tend to adopt them wholeheartedly. Then, with time, they realize they are not quite as good as they thought they were and that there are sobering complications. DES probably fall into that category. Initial reports of zero restenosis are not quite true. It depends on the individual, the vessel, and other co-morbidities, but restenosis can be as high as 15%-17% (with DES) in some vessels and individuals. And, while the overall acute stent thrombosis rate is probably no different (with DES) than for bare metal stents, for bare metal stents it is predictable because it occurs within 1-2 months, but with drug-eluting stents it is unpredictable and can happen almost any time. And it can happen very late, and that makes people a little nervous – at least it makes me nervous. Dr. Renu Virmani (a noted pathologist) has always been worried about whether we are delaying restenosis (with DES), and that does not seem to be borne out, but the late thrombosis is a concern."

So far, there have been no reports of stent thrombosis more than 30-days post-procedure with Endeavor, which elutes zotarolimus from a phosphorylcholine-coated Driver stent. If that holds up over time, it could be a message that will resonate with cath labs and cardiologists. However, sources asked about Endeavor who have not yet used it in a clinical trial are withholding judgment. A cardiologist said, "It's hard to say what I'm most excited about until I get the new stents in my hands. Endeavor is a nice, deliverable stent, but the late loss is high. It is possible that restenosis is a combination of the stent (design) and late loss. From a bare metal stent stand-point, Driver had the lowest restenosis rate, so Endeavor's high late loss may not make any clinical difference. I'm somewhat cautiously optimistic about Endeavor…Conor's CoStar is intriguing but who knows whether the cups in the stent (reservoirs filled with paclitaxel) will do the job?... Abbott's ZoMaxx (which elutes zotarolimus from a TriMaxx stent coated with phosphorylcholine) is awfully good, and so is Xience (an everolimus-eluting stent to be sold by both Boston Scientific and Abbott)…It's exciting because the market will be very competitive, and I think prices will plummet. I think in seven years we will see drug-eluting stents for $200."

♦