

Stenting for Coronary Artery Disease: Panacea or Placebo?

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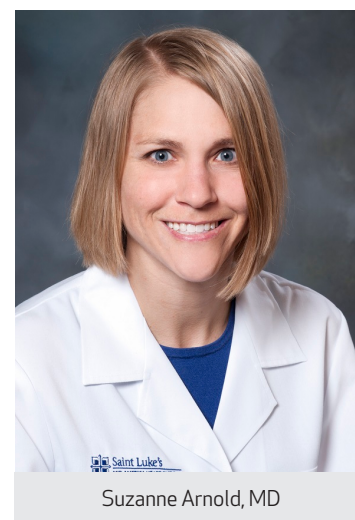
After suffering a heart attack at last year's American Heart Association (AHA) Scientific Sessions, AHA president John Warner had a stent inserted as part of his treatment. The procedure was not unusual, with stenting being the appropriate therapy for myocardial infarction (MI), but the news coverage was. At least one headline reported that Warner had undergone a "stent procedure no better than placebo." Thus defines the cardiovascular controversy of the 21st century: compared to medical therapy, is stenting a placebo or an antidote for heart disease?

For decades, stenting has been the go-to tool for treating patients with coronary artery disease (CAD). It's a logical assumption: if a blocked artery is bad, then opening it must be good. A recent string of clinical trials, however, has called this long-accepted practice into question—at least for stable CAD. Mounting evidence suggests that stenting for stable CAD may be no more effective than optimal medical therapy when it comes to prolonging life, and the improvement in symptoms may be little more than a placebo effect. The news has sparked a heated debate in the cardiology community, challenging decades-old norms for physicians and patients alike.

DEBUNKING CONVENTIONAL WISDOM

The controversy took off in 2007 when COURAGE trial investigators announced that after comparing the results of 2,287 stable angina patients randomized to optimized medical therapy with or without percutaneous coronary intervention (PCI—or stenting), PCI showed no improvement over medication in terms of morbidity and mortality. Subsequent studies confirmed COURAGE's results, albeit raising questions about the generalizability to patients with higher plaque burdens, multiple colluded arteries, and so on. However, the biggest shock came in 2017, when the results of ORBITA, the first sham trial of stenting for stable

CAD/angina, were announced: Investigators found that patients with stable, single-vessel disease who had stents placed had no more improvement in symptoms than patients who received the sham procedure. The news reverberated through the cardiology world—could the benefits of stenting be due to a placebo effect? "ORBITA was a shocking study. We as a community have long felt that an open artery is better and that we're saving people's lives by stenting them, even in the setting of stable coronary coronary artery disease," says Suzanne Arnold, M.D., cardiologist at Saint Luke's Cardiovascular Consultants in Kansas City, Missouri. "We've been operating under that assumption for quite some time. We are now realizing that a lot of those things we have believed for a long time probably aren't true, but we still hold on to those concepts."



Suzanne Arnold, MD

THE RISE OF STENTING

"To understand the impact of COURAGE and ORBITA, you have to look back at the history of how revascularization became part of our world in cardiology," says Arnold, who wrote a review on stenting for CAD in the latest issue of the Methodist DeBakey Cardiovascular Journal. "We went from bypass surgery as the standard for treating acute MI to this much safer, minimally invasive stenting procedure that was giving our patients huge benefits. Moving downstream from stents, everything else became safer. It's hard when something has become engrained in practice to then go back and challenge whether or not it's effective."

Stenting rose rapidly to prominence in the 1990s as a less-invasive alternative to coronary artery bypass grafting (CABG) surgery for some forms of CAD or acute MI. Rather than cracking open the chest, physicians could safely deliver a tiny mesh stent via a catheter snaking from distal vessels to prop open a plaque-clogged coronary artery and restore blood flow to the heart—a process called percutaneous coronary intervention (PCI) or angioplasty. Studies in the 1970s and 1980s showed that revascularization by CABG had much better outcomes than the medical therapies available at the time. When stenting came along, offering a faster, safer method of revascularization, the benefits were assumed to carry over to the new technique—an assumption that went largely unquestioned for years.

However, there is a caveat to this assumption: Procedures weren't the only things to improve in the 1990s; medicine was improving, too. The medicines available to treat CAD at the time of the original studies were not nearly as effective as the ones available by the turn of the century. Until COURAGE, modern medical therapy and stenting never had a head-to-head test.

That is, until COURAGE and ORBITA.

QUESTIONS AND CONTROVERSY

"Before ORBITA, the possibility of stenting having a placebo effect was not really talked about that much," says Arnold. "Every cardiologist personally has a wealth of anecdotal data that says my patients feel better after stenting, so it's really challenging when someone suggests that it could in part be a placebo effect. Then we say, 'Well, I know placebos are real, but I know my patients feel better after stenting.' Well, yes, they do, but..."

That "but" drives much of the debate about the generalizability of these clinical trials. Critics point out that ORBITA was only tested on low-risk patients who had single-vessel disease and few angina symptoms to begin with, so its results can hardly be generalized to a broader, high-risk population. COURAGE had similar flaws, enrolling few high-risk patients and using what some critics alleged was a substandard PCI technique with minimal use of drug-eluting stents. Even after several follow-up studies, the roles of stenting and medical therapy for patients with high-risk ischemia is still an open question. However, others point out that there isn't any evidence supporting the current guidelines to use PCI for stable CAD either,¹ making ORBITA the fatal blow to the assault COURAGE began.

"There's been a lot of conversation about this among my colleagues. Particularly since ORBITA was released, I have had cardiovascular surgeons asking me, 'What do you

think of all this?'" says Arnold. "It's interesting to see that most people fall on the side of not wanting to believe the results. Again, we all have years and years of anecdotal evidence that counters this. Anytime you go against something that has been a long-held belief, it's hard on both sides."

Arnold now favors a more cautious approach toward stenting, preferring to maximize medical therapy before risking the side effects of stenting—which, although less risky than CABG, is still associated with low risks of myocardial infarction, renal injury, stroke, vascular complications, and even death. Even so, she acknowledges that the debate is far from settled.

"Both studies have criticisms that are valid. For instance, ORBITA was underpowered for its analysis of quality of life benefit and had a very short follow-up. There are a lot of physicians who truly believe that stents are important and are helping their patients, and they get hung up on the issues with the trial and why it doesn't apply to their patients," she says. "I still don't think stenting is dead. I think there is absolutely a role

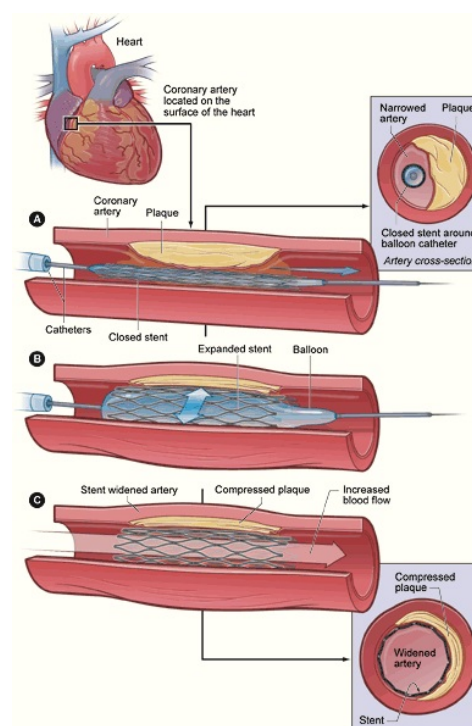


Diagram of stent placement. In A, the catheter is inserted across the lesion. In B, the balloon is inflated, expanding the stent and compressing the plaque. In C, the catheter and deflated balloon have been removed. Before-and-after cross sections of the artery show the results of the stent placement. (Source: National Institutes of Health)

for stents and revascularization in stable angina, but I do think that ORBITA really does highlight that there's a placebo effect for many people.

WEIGHING OPTIONS WITH PATIENTS

Given that physicians and experts have such conflicting understandings of stenting, it's even more challenging for patients to understand its benefits and risks. Over the years, the ideas that stenting is the best treatment and blocked arteries will lead to heart attacks have trickled down from doctors to patients. As a result, many patients with CAD come in expecting to receive stents—which may not be the appropriate treatment according to the latest evidence. It is particularly difficult to explain the change to patients who have had a previous heart attack, Arnold points out.

"It is confusing because we tell people different things—based on appropriate data—depending on if you're in a setting of a heart attack or not," Arnold said. "A blocked artery with a heart attack is an emergency, and we treat it appropriately. But a blocked artery that has closed up over time and people have grown accustomed to it is not an emergency. It's difficult to make patients understand that."

The media has also made this mistake, leading to confusing and misleading headlines. Take, for instance, the headline that likened AHA president John Warner's stent procedure as "no better than placebo." Warner's MI came just after the ORBITA trials about stable CAD made the news, and even though stenting was the appropriate treatment for his condition, the headline confounded two very different diagnoses.

To explain that stenting is not necessary to treat all blocked arteries, Arnold tells her patients that a blocked artery is not a "ticking time bomb in their heart." She also explains that medicines are the key to preventing heart attacks and keeping patients alive, and that stents will not change a patient's likelihood of suffering a heart attack. She is also careful to correct the common misconception that stents (or medication) represent a cure.

"I think it's a matter of continuing to talk to patients, telling them 'You have coronary disease, and we're managing it with these techniques, and stents are one tool that we have.' I try to explain to my patients that the cholesterol plaque in their hearts that we treated with a stent can build up in every vessel in the body. That's why medications and lifestyle changes are so important, because the stent may open one artery, but that plaque process is happening everywhere," Arnold says.

Regardless of the tools physicians and patients choose to use, Arnold emphasizes that mortality and morbidity—the

points emphasized in COURAGE—are not the only outcomes that matter. ORBITA has not completely erased the notion that stents may make patients feel better, even if their risks of heart attack or death remain the same as with medicine.

"I absolutely believe that maintaining and improving quality of life is extremely important," she says. "I just want to make sure that they understand why we're doing what we're doing. I discuss with my patients how medicines can also be very effective at improving quality of life, and sometimes not exposing you to the risk of a procedure may be important as well. It's really difficult because we don't really know how much quality of life improvement is from stenting or from placebo effect."

So, to stent or not to stent? The verdict is still out for patients with stable CAD, and the decision must be made on a case-by-case basis, depending on the physician's judgment and patient's needs.

As Arnold puts it: "This is a nuanced issue, which is a difficult thing for both patients and providers to deal with. Things that are black and white are so much simpler."

Conflict of Interest Disclosure

Laura Gerik is assistant managing editor and Ryan Chang is an intern at the *Methodist DeBakey Cardiovascular Journal*.

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