BroadcastMed | Bare-Metal, Drug-Eluting, and Bioresorbable Stents in Context

RAJIV GULATI: Greetings. I'm Rajiv Gulati, Interventional Cardiologist at Mayo Clinic in Rochester, Minnesota. And today we'll be discussing what's new in bare-metal and drug-eluting stents. I'm joined today by my colleagues Dr. Gurpreet Sandu, Director of the Cath Lab at Mayo, and Dr. Malcolm Bell, Director of the Ischemic Heart Disease Program. Welcome gentlemen.

MALCOLM BELL: Thank you, Rajiv.

RAJIV GULATI: Thank you. Malcolm, maybe I can start with you. Why don't we start with NORSTENT? Tell us what basically the study was, and the headline findings?

MALCOLM BELL: Well, NORSTENT, as we all know, was just recently presented and then published just in the last few weeks. I think it's important though that we understand the historical context of this trial. Remembering that drug-eluting stents were developed to overcome the failings of bare-metal stents over many years. Early on, was a concern about an added risk though with drug-eluting stents, even though they reduced restenosis, because of the issue of stent thrombosis.

RAJIV GULATI: First-generation of--

MALCOLM BELL: First-generation drug-eluting stents. So we're talking about the CYPHER and the TAXUS stents in particular. And then, over time, with second-generation drug-eluting stents, it became apparent from a number of meta-analyses that perhaps these stents were actually safer than bare-metal stents.

But it's not really clear that that message was really heard by everyone in the field. But, certainly, recent guidelines have suggested that drug-eluting stents are superior to bare-metal stents. And that that safety issue is no longer important.

Some of those analyses actually suggest that there was a decrease in MI and mortality with drug-eluting stents, even though we have--

RAJIV GULATI: With the current stents.

MALCOLM BELL: With the current drug-eluting stents. And that's always been a little difficult to fathom out. So that was the background.

And the NORSTENT was a large, really well-conducted Norwegian study. They enrolled probably 60% or more of all of the PCI procedures that were done in Norway between about 2008, 2011. And they randomized them to a bare-metal stents and drug-eluting stents. And they took all comers.

So that's really important. Because that reflects our common practice. And using stents that we're using today. So a very, very important study, and I think they need to be congratulated for that.

But that was a randomized study, performed in every stent center in Norway. It's the largest bare-metal stent versus drug-eluting stent study ever performed. Over 9,000 patients.

And getting back to your original question, the headline news was that the primary endpoint-- this is important to everyone to understand-- was MI and mortality. And it showed that these were equivalent.

Now, some people would be surprised by that, but we really shouldn't be, because we've never shown that stents have improved survival, and why would it necessarily decrease MI. But particularly, that survival question. So I think that was very clear from this study.

However, the secondary endpoints were target vessel revascularization stent thrombosis. And it was very clear that drug-eluting stents were superior in both of those endpoints, compared to bare-metal stents.

And so it really showed that drug-eluting stents, second-generation stents, are doing-- are performing better than bare-metal stents. And, in particular, the stent thrombosis was reduced and revascularization was reduced, which is exactly why these stents were developed in the first place.

So I think this is really good news for all of us who are using the second-generation drug-eluting stents.

RAJIV GULATI: Very good. Gurpreet, if I can turn to you. I mean, so the primary endpoint was neuter, wasn't negative, but the rates of TLR were lower with the second-generation drug-eluting stents. Clinically meaningful? Economically meaningful?

GURPREET SANDU: I think this is clinically meaningful, because, as you know, the differences were 5% TLR for the drug-eluting stents.

RAJIV GULATI: That's the absolute reduction.

GURPREET SANDU: Yes. Versus 10% for the bare-metal. So that is a substantial difference. And pretty much goes in line with what we know about drug-eluting stents and why they were designed.

Similarly, as Malcolm mentioned, the stern thrombosis rates were about 0.8% for the drug-eluting stents versus 1.2% percent for the bare-metal. So both were equally good, but very nice reassuring results overall.

RAJIV GULATI: Let me ask you one more thing on this study, Malcolm. The diabetics were under-represented?

MALCOLM BELL: Yeah. So, as I said, it was all comers. And there were very few exclusion criteria, so if you'd had a prior stent, you weren't allowed to be in the study. And a few other things there that would make sense.

And the typical breakdown standard/nonstandard unstable angina, stable angina. But the diabetics, it's interesting. There's about 12% of the population in this study had diabetes, which is at least half of what we typically see in these stent trials. So I think we just have to be a little careful with their interpretation. Although there was no signal that these were doing-- one was doing significantly better in one versus the other.

RAJIV GULATI: But you think they were underrepresented because they weren't randomized? The clinicians had concern about randomizing diabetics to bare-metal stents?

MALCOLM BELL: I don't think so. That didn't-- that wasn't really apparent to me. The other thing, too, is that this was a relatively younger age group. So, as I said, you enrolled a lot of people having stent procedures in Norway during that time. And yet, the median age was a little lower than what we might typically see.

But the diabetic-- your question is important, because, as we know, drug-eluting stents, at least for the first-generational studies did seem to perform much better in diabetics, compared to bare-metal stents.

And there's one other thing. You know, I think that maybe this will come out. And Gurpreet can make some comments on this, as well. But is that drug-eluting stents were introduced about 13 years or so ago. And we tend to keep comparing drug-eluting stents that we are currently using to the old bare-metal stents. But we have to remember, bare-metal stent technology has improved, as well.

So these bare-metal stents were really, as we say, the second-generation of drug-eluting stents are not your grandfather's bare-metal stent. So these are your different alloys, thinner struts, and, in fact, many people may be surprised at how well bare-metal stents actually did in this study, but yet drug-eluting stents still outperformed them, with respect to the secondary endpoint.

RAJIV GULATI: OK. The stent thrombosis rate though was statistically significantly low with the drug-eluting stents, which I think really solidifies what we've learned from some of the meta-analyses. Fascinating findings. Any thoughts, Gurpreet, as to why the current generation DES may have lower late stent thrombosis rates than the bare-metal stents?

GURPREET SANDU: Yeah, I think there are basically several improvements that have happened over the years. The first improvement we've seen as the strut thickness. So the original CYPHER stents had pretty thick struts. There was also some risk of the polymer fracturing, and causing stent thrombosis. So that is pretty much gone away.

And the current generation drug-eluting stents and bare-metal stents, like Malcolm said, are a completely different platform. Lower profile, thinner struts. And even the quality of the polymers is better.

RAJIV GULATI: And then with regards to the stent thrombosis, it's maybe worth pointing out that in the NORSTENT study, both bare-metal and drug-eluting stent groups received nine months of a dual antiplatelet therapy. And when we think about bare-metal stent utilization in the US, it is typically to abbreviate the duration of antiplatelet therapy. Any comments on that

MALCOLM BELL: Yeah, that's a great point to bring up. I think we have to be very, very cautious in our recommendation of shortening the length of antiplatelet therapy for bare-metal stents with the belief that we're going to reduce the rate of any event, if we put a bare-metal stent in versus a drug-eluting stent.

So you're absolutely right. Nine months of dual antiplatelet therapy. So I think that we have to be very, very careful in extrapolating this to say that we can put a bare-metal stent in and just giving a very abbreviated course of dual antiplatelet therapy.

And, again, I think the point of this study that is really important for us to remember for the finding, is that this stent thrombosis rate, and it was actually very low in both groups--

RAJIV GULATI: Right.

MALCOLM BELL: So I think therein lies the point that the technology has changed significant for both stents. And, again, survival wasn't any different.

But I think that, and certainly based on the meta-analyses prior to this study, I think there was a warning there that we shouldn't underestimate the benefit of putting a drug-eluting stent, and that there probably isn't that upfront risk of stent thrombosis exceeding what it would be for bare-metal stent. If that makes sense.

RAJIV GULATI: Yeah. No, I think that that's very helpful. It does make sense. So any role for bare-metal stent in your practice nowadays with the NORSTENT study? Which patients might you expect to use bare-metal stents in?

MALCOLM BELL: I think, in general, most patients should be considered for drug-eluting stents. I think NORSTENT really shows us that there's no downside to putting a drug-eluting in. And, furthermore, we've had recent data and guidelines supporting shorter duration of dual antiplatelet therapy, three to six months, particularly for patients with stable angina.

But the patients who you might consider bare-metal stent and if cost was an issue. That's not usually an issue in this country. A very big vessel, where we may need to put like a five millimeter bare-metal stent. And the incidence of resources there is very, very low.

I think the question of the patient who's at risk of bleeding is still open. And, as you pointed out, bare-metal stents in this study still were accompanied by nine months of dual antiplatelet therapy. So we don't know whether, in this type of population, with these stents, whether each stint would perform the same, particularly in terms of safety, with shortened dual antiplatelet therapy.

RAJIV GULATI: Well, that's a nice transition. Perhaps we can move on to another study, the patients with high bleeding risk and possible potential to reduce DAPT duration. Gurpreet, you want to comment on the LEADERS FREE study. Give us the headline news and the design?

GURPREET SANDU: So the LEADERS FREE study was basically biolimus A9 or umirolimus versus the bare-metal stent. And these received 30 days of dual antiplatelet therapy.

RAJIV GULATI: Now, we don't-- these are not FDA-approved to be utilized in the US.

GURPREET SANDU: Yes. These are not available in the US. And these stents are also polymer-free, surface drug on the metal versus bare metal. And 30 days, about 1,200 patients in each arm. And the results here were fairly in-line with what we know of drug-eluting stents versus bare metal stents. About 5% versus 10% target lesion revascularization.

But there was something interesting in here. Stent thrombosis rate in both arms were about 2%. So maybe this is something, Malcolm, that you could comment on.

MALCOLM BELL: I think it's a higher risk population, and we still don't know what the minimum duration of dual antiplatelet therapy. But these are complicated patients. There's all sorts of reasons why they may have a higher risk of stent thrombosis.

RAJIV GULATI: And these specifically were higher bleeding leading risk patients. They were elderly. They had other risk factors.

MALCOLM BELL: Right. You know, and then they need to have some surgery. So there's something else about these patients. So we know that, yes, they are a high risk of bleeding. And that's a problem in itself.

GURPREET SANDU: Yeah.

MALCOLM BELL: And this slightly higher risk of stent thrombosis. But it's hard to sort of tease out what comes first. And so we don't really know the circumstances, at least what has been published, on what the stent thrombosis were.

But, I think, again, it tells us that we don't have to necessarily put bare-metal stents into these patients. The patients who got the drug-eluting stents still did better.

GURPREET SANDU: But is there a fine line between three months of DAPT versus pushing it down to one month for the drug-eluting stent?

MALCOLM BELL: I think that remains to be seen. It really does.

GURPREET SANDU: Yeah.

RAJIV GULATI: Very good. Well, we discussed nicely the NORSTENT trial, that bare-metal versus drug-eluting, and we've alluded now to the LEADERS FREE study. Why don't we move on to bioabsorbable scaffolds. The hot topic of the day. Exciting promise for the future.

Gurpreet, you want to comment on maybe some of the recent findings that were presented at TCT a couple of months ago?

GURPREET SANDU: So at TCT, the main discussion was the three year data on the Absorb stent.

RAJIV GULATI: The ABSORB II trial, three year follow up.

GURPREET SANDU: Yes. Three year follow up. And the one slight red flag there which raised concern was the late stent thrombosis rates with these. There were about six patients who develop late stent thrombosis out of about 300 plus patients. And that was concerning. There was the control arm, which was the drug-eluting stent, there were no late stent thrombosis.

RAJIV GULATI: Malcolm, any comments on those findings? They have not been published yet, as far as I understand.

MALCOLM BELL: Yeah, so it's a promise, isn't it? And I think that intuitively, and all of us, all of our patients, would love to walk in and say, if I have a stent that dissolves away, there is no evidence of it being there in one to three years, that would be wonderful.

And although these trials are meeting their primary endpoint, there is this warning signal of higher rates of later stent thrombosis, which will throw the whole duration of DABT into confusion, I think. So we don't know the answer to that.

We know, and just-- we know there are some issues in terms of deliverability. Are we choosing the right size for the stents? One of the concerns in the FDA-- I mean, it been approved in the United States. They had these data. And they-- and they don't have all of it, of course, but when it was approved, they had the data that still showed a signal of these later events being more frequent with the bioabsorbable vascular scaffold.

But it may be that these were just in the smaller vessel. So I think we have to be careful. And one thing which is really interesting, and one of the promises was that this would maintain, or at least you could have vasomotor function restored, where you generally don't with a bare-metal stent, because simply there's a bare-metal stent there, or a drug-eluting stent. So a metal scaffold, of course, that isn't going to vasoconstrict, vasodilate.

And, interestingly, in the ABSORB II trial it showed that there wasn't a difference. And that's a little disappointing. So I think there are going to be a lot of challenges for us, and our patients, trying to choose who's going to want to have these stents. Who should we put these in? But there's a--

RAJIV GULATI: Just to counter that, I MEAN just to get to play the devil's advocate, there have been concerns or questions about methodology. What we certainly learned from the earlier ABSORB studies that deployment matters, technique matters, and that has the potential to influence long-term outcomes. Method of assaying vasomotion. There's multiple different ways.

And perhaps, as we see these data come out into the public domain, we'll be able to tease out some of the nuances of the trial, and how methodology may have impacted long-term outcomes.

MALCOLM BELL: I think that's true. And it just goes back to those early drug-eluting stent days, isn't it?

RAJIV GULATI: Yeah.

MALCOLM BELL: We just got a little lazy in terms of putting these in. And--

RAJIV GULATI: Right.

MALCOLM BELL: And so, again, we haven't used these in the United States for very long at all, so we don't have a vast experience. And speaking to people who have had a lot of experience, implantation technique is going to be absolutely critical. So we cannot afford to get sloppy with these stents.

But there will be some more longer term data coming up, with the ABSORB IV trial. And we're all hopeful that these will be reassuring. But at the moment, I think there are some warning signals. Not enough to say that we shouldn't just use them carte blanche, to just make that decision.

And I think we've got to keep an open mind here. But it may be mean-- I mean, these are first-generation. But I'm not sure that we're going to see second-generation absorbing scaffolds that are going to look very different to this any time really soon.

I mean there may be some other-- also, Gurpreet has on other types of reabsorbable stents. So we're talking about an absorbable scaffold, but there are absorbable polymers, and so this can get very confusing for the average person who's not dealing with these stents.

GURPREET SANDU: Yeah. I think, at this time, this is the first-generation bioabsorbable stent. The struts are pretty bulky. The deployment technique needs to be absolutely perfect.

And then one thing we do need to remember is it doesn't disappear within a year. There are fragments that may take up to two years or three years to disappear. Those are pseudo-thrombogenic. And it doesn't expand the same way as the metal stent, where you inflate it with a balloon. It stays open here. It's a stepwise careful denotation. So mechanically, it' different. And--

RAJIV GULATI: I think that's a very fair point. This is first-generation BRS technology, compared to what you both have already described as the best in class, second-generation, super outcomes DES that we have. And perhaps moving forward with more data, we'll see things change.

MALCOLM BELL: I think we need to be very, very careful though in our patient selection. And so we are about to have these introduced into our own practice. And I think we're going to have to work out who the patients that are going to be ideal for this, and who are the patients that we need to avoid.

And obviously there are some lesion specifics that we may want to avoid. But it may be that elderly patients, with the older patient who has lots of other co-morbidities in issue, it may be that the benefit of having an absorbable stent is not as great as it might be for a younger person.

And I don't know how we're going to tease that out.

RAJIV GULATI: That's the sweet spot, yeah.

MALCOLM BELL: But I just don't think you suddenly change your practice and stop putting DVS into everyone.

RAJIV GULATI: Well, gentlemen, thank you for your very important insights today about new developments in stent technology and stent comparisons.

And thank you for joining us on theheart.org on Medscape.