

## **BroadcastMed | Revascularization with PCI or CABG in the Post-SYNTAX Era**

**JAY WIDMER:** Howdy I'm Jay Widmer, interventional cardiology fellow here at Mayo Clinic Rochester. During today's recording, we'll be discussing PCI versus CABG in the post-SYNTAX era. I'm joined by two mentors, Dr. David Holmes interventional cardiology pioneer and Dr. Lyle Joyce, cardiovascular surgery here at Mayo. Welcome to you both. We'll go ahead and get started. And we'll start with you, Dr. Joyce. Based on two of the recent trials in the SYNTAX trial, how can there be such striking differences in terms of the results and the reportings in such well-designed trials?

**LYLE JOYCE:** I think we need to look at several different facts in considering what went into the design of the trials and also the timing of the trials. The SYNTAX trial, for example, I think completed its enrollment in 2007 whereas the EXCEL and NOBLE trials are much more recent than that. In that period of time, there has been a marked improvement in PCI and stent technology. So I think to compare something that is 10 years earlier with the technology we have now is likely going to give some varying results. There's also some differences in the definitions, for example what constitutes an MI. Also a little difference in what groups of patients were studied as far as the EXCEL trial looking more at the left main with low risk SYNTAX scores as opposed to the others.

**JAY WIDMER:** Exactly and going with that left main subpopulation Dr. Holmes, who do you think is a candidate now for left main coronary PCI based on the results of these trials?

**DAVID HOLMES:** I think that's a really important question, depends upon what the specific metrics are that you're going to use to talk with the patient about. I think those patients that are probably optimally suited for dilatation of left main disease would still be those with ostial lesion and trunk lesion. Bifurcation disease, distal bifurcation left main disease is clearly treatable, although it's much more complex, as you know. And I think the results are not as good as with more isolated left main disease. I think isolated left main disease in the absence of other complicating factors of complexity of coronary disease is very well treated with PCI as well as with surgery.

There is a difference between the two. One of the endpoints that is important is that all the data on surgery except for the NOBLE trial, would indicate that stroke is increased with surgery as compared to dilatation. Now, the difference is statistically significant but it is small. There isn't any question about that.

The next piece of information is to say as the lesions get more complex, as the complexity of disease increases further, the SYNTAX trial identified the fact that more extensive disease is better treated with coronary bypass graft surgery. I don't think these trials have really changed that or moved the needle. I think those patients that have extensive multivessel disease, that cannot be treated with intervention, those patients that have LV dysfunction, those patients are still better served by acquiring surgery in terms of the overall composite end point.

**JAY WIDMER:** Exactly. Exactly. Well, Dr. Joyce heading back to you, in terms of the newer trials, for you, did you have any changes in your practice based on NOBLE and EXCEL versus what we saw in SYNTAX?

**LYLE JOYCE:** No, I think our practice has continued pretty much the same. You know the fact is, if you really sort out the details of the EXCEL trial, for example, it was looking more at the patients with a low SYNTAX score. And if you look at the results of the SYNTAX trial, in the low SYNTAX core group, they're not that much different than the EXCEL trial

**JAY WIDMER:** Right.

**DAVID HOLMES:** So there's an interesting-- I hate to interrupt. There's an interesting issue. We have really relied on the concept that arterial revascularization would be better than anything. So we then said, gosh, if there is one artery that's really good, the LIMA. If you were to add a second artery, the RIMA, that the results would be much better than a LIMA plus vein grafts.

And so, it was surprising to see the literature of the recent trial that found that there isn't any difference between one mammary and two mammaries. Which was surprising, because we always said, gosh the reason that SYNTAX surgeons didn't do as well, as you might have thought they could have been better, was that most of the time they just used a single mammary. The same was true in NOBLE and EXCEL. We might then say, gosh-- or we did say, if you had used two mammaries, they would do much better. And yet, the trial showed that you many any difference if you use one or versus two. Can you talk about that?

**LYLE JOYCE:** Well, I think we have to go back to some of the original studies at looking at what keeps vessels open. And there's no question, but what a graft to the left anterior descending coronary artery has a higher long term patency rate than any of the other the circumflex or the right coronaries. So, I think to expect a RIMA to the right, or to the cimcumflex, to be equal to the left internal memory down to the LAD, probably isn't justified. I mean it's-- part of it is just the runoff and the makeup of the vessel and the disease of the vessel. So we certainly believe that all arterial grafting is the way to go. But it does--

**DAVID** We just can't prove it.

**HOLMES:**

**LYLE JOYCE:** Well.

**DAVID** But other than that.

**HOLMES:**

**JAY WIDMER:** Do you think that we're not quite at the end point for that? We were looking at five year results for the recent trial that you noted. At 10 years, do you think we'll see any difference?

**LYLE JOYCE:** Well certainly it's been shown that the left internal memory to the LAD has a striking difference in 15 plus year patency rates. So, I think you're right. If we get out past the perioperative period the first year, and look down the road 10 or 15 years, we probably will see an improvement in bilateral mammaries and perhaps all arterial. The radial is a little less dependable than the right internal mammary.

**DAVID** One of the problems that you've talked about is as we get to 10 and 15 years, by the time we look at 10 and 15 years, all the technology has changed because it's 10 or 15 years old. That was seen in SYNTAX. In SYNTAX, for example, we used a drug-eluting stent that is not even manufactured anymore. It's not nearly as good as what we currently have, but we didn't have that better stent when the SYNTAX trial was started.

And so, looking at long term data is always complicated by that.

**LYLE JOYCE:** Definitely.

**DAVID** Surgical techniques get better, and interventional techniques get better, and so does that mean that what we should do is to focus on concepts of complete revascularization or concepts of using an arterial graft irrespective of whether it's single or dual mammaries or radials versus using percutaneous techniques that just treat a small segment of the artery? There are lots of different things to talk about in that regard.

**LYLE JOYCE:** There are. In fact, going back to the SYNTAX trial, that was one of the problems with PCI was the inability to completely revascularize. And actually there was that subgroup that looked at the residual SYNTAX score. And if residual SYNTAX score was over 8, then the prognosis was worse. So yes, I think those elements are important, but you're absolutely right.

It is very difficult to compare 10 year data from a stent that's not even around anymore. It's perhaps a little bit more reliable, in the surgical technology, because the only variable there at the present time that we have made really has been two things. One is whether we use all arterial or not, and then whether it's on or off pump. Otherwise, our techniques are pretty much similar to what they've been 10, 15 years ago.

**JAY WIDMER:** So I'd like to talk about some of the technologies in a little bit, but going back to the residual SYNTAX score, we saw even with EXCEL, the on-site calculated or estimated SYNTAX score was much lower than the core lab. It's a difficult thing to come up with, and sometimes are doing these things on the fly. Do you think that the SYNTAX score is something that we can integrate into our practice, I'll throw it to either one, integrate into our practice easily what are some ways we can use that, or should we be looking somewhere else?

**DAVID HOLMES:** I could take that. It is terribly important that the practice of interventional cardiology has changed and continues to change. It used to be the concept of dilatation sort of at the time of diagnostic angiography was something that, first of all, it's very popular with patients. But second of all, the professional societies have backed away from that. And I think that that is important in that regard.

In fact, Europe has led the way in that. If you have a patient that has elective symptoms, that you're considering elective revascularization, so the patient that has relatively stable angina, if they have multivessel disease, by mandate, they're taken off the table, and then the heart team is brought together to review things. In that system then, you can calculate a SYNTAX score. It's not like you have to do it on the fly. You have a chance to do that.

Now having said that, there is some pushback from patients. They'd rather not come back to the laboratory. They'd rather not have two procedures. However, having said that, it's such an important decision, that I think that the heart team to truly in all of its manifestations invoke that and bring that to play is a terribly important point.

**LYLE JOYCE:** I agree. I think it is complex, and it's difficult for the patient to understand. But I think the most important thing for the patient to know, is that there is a heart team that's looking at it, which comprises members on both sides of the table, surgical as well as cardiology. And I think that's the assurance that the patient needs, that when both groups have looked at it and decided, on the basis of SYNTAX or other elements that are involved, that the recommendation is a combined recommendation. The surgeon, for example, is going to look more at things like what's the-- how much problem does the patient have with COPD or renal failure, you know the other co-morbid problems. The cardiologist is probably going to look more at the anatomy, how much calcification is, the chronicity of occlusion, those sort of things that make a technical difference. It's important the patient knows that all those things have been factored into the recommendation that was provided to him.

**DAVID HOLMES:** So what, we talk about being patient centric care. So have a heart team. Then we have the patient as part of that. As we talk with patients, it's very hard for them to keep in mind the issue that there is a difference in maybe a hierarchical endpoint of stroke versus repeat revascularization versus death versus myocardial infarction.

There are some patients, when you talk to them and say, Josh, the survival at five years is the same. And that is true, in most of the trials. But there is a difference in repeat revascularization and a difference in myocardial infarction and a difference in stroke. The patient then typically says, well tell me about this stroke thing. Because that's the thing that I fear the most. And so, then while you can present stuff to the patient, the patient's attitude winds up really coloring many different things. How do you approach that?

**LYLE JOYCE:** When I discuss it with the patient, I try to get them to focus on two differences. One is, the long term benefit versus the short term benefit. I try to explain to them that, yes when you're talking about stroke and MI and those sort of things, you're sort of taking more of the risk up front, with going surgical route.

Whereas, if you're looking at the long term outcome, then maybe you have to weigh in a little bit more. OK, is it more important for me to sort of get over this hump and then know that I'm not going to have to worry about anything for a longer period of time. Or is it more important to me to just have the least invasive approach taken right now, and I'll worry about that later. It's interesting patients are different aren't they.

**DAVID** Extremely.

**HOLMES:**

**LYLE JOYCE:** One patient is adamant that there is no way I'm ever coming back. "You better do whatever you are going to do that's going to fix me for the rest of my life." And the next one is going to say, "boy if I don't have to go to surgery, just fix me up simply as you can. We'll worry about that later."

**DAVID** That last patient, and having been in that circumstance, to take the short term option, because then they immediately say, "well in five years I would have been exercising like crazy. For sure I will have stopped smoking, and my blood pressure is going to be perfect. So there's lots of things I can do that will impact, I think. Having said that, most of the time, that doesn't happen because at five years, we're still about as heavy as we are now.

**JAY WIDMER:** You bring up a good point about optimal medical therapy, smoking cessation, exercise, that sort of thing. And you are an author on a paper with Iqbal and colleagues about optimal medical therapy in this SYNTAX trial. Curious if you have thoughts, if optimal medical therapy in some of these newer trials will have an impact, or could have an impact on some of the outcome, and how can we use that to weigh into some of our patient-centered decisions?

**DAVID** Sure. I think that the concept of optimal medical therapy is incredibly easy to say. I think the implementation of that is incredibly difficult because it involves multiple different things. It involves the economics of taking pills for a long time. It involves the issue of willpower, which as we know lasts for 30 days and is soluble in alcohol, and a whole bunch of other things in terms of side effects for drugs. And so, when we put patients on optimal medical therapy that includes losing weight and exercise and stopping smoking, and taking medications every day, boy at five years, the number of patients that are able to do that is really limited. It would be just like saying the Ornish diet is a great diet, you have to just eat dandelions. I'm not sure exactly what that means. And the number of people that can do that, do incredibly well. It's just that that's a small number of people. And so optimal medical therapy is a great goal, terribly important, but we don't have very good strategies for that.

**JAY WIDMER:** Absolutely.

**DAVID** I don't know. Maybe you have better strategies. in the surgical wing.

**HOLMES:**

**LYLE JOYCE:** Well, unfortunately, you know I'm disappointed in our surgical colleagues in the SYNTAX trial. I mean the failure to continue with optimal medical treatment was far too low in that surgical arm. We know it's beneficial. There's no question about it, if are on at least a single platelet inhibitor and a statin and a beta-blocker and an ACE inhibitor. But you're right. It just isn't followed as completely as it needs to be. Even knowing that the outcomes are somewhat better.

**DAVID** One of the problems is that patients come in with a heart problem, and they think you're going to save their life.

**HOLMES:** And then you revascularize them with surgery or dilatation. And at that point in time, it's very hard to get the message across saying, We have not eliminated the need for medications.

**LYLE JOYCE:** Right.

**JAY WIDMER:** Right.

**DAVID** And it's not going to last forever.

**HOLMES:**

**LYLE JOYCE:** That's right.

**JAY WIDMER:** So looking down the road, five, 10 years, in terms of stent technology, surgical technologies, what do you all see as things that might turn the corner for some of these or be game changers in terms of things we will do in five to 10 years? Dr. Holmes?

**DAVID** So, I think you could include that, then some of the new medications that are coming along, the PCSK9 drugs in which compliance may not be as big a problem, because it could be once a month, or once every two weeks, or it could be a vaccine. If indeed that works--

**JAY WIDMER:** Right.

**DAVID** --that will be a huge game changer. Now, nobody knows whether that's going to work or not. But that's the sort of thing that could, number one, improve compliance, if you can afford it.

**JAY WIDMER:** Cost is going to be huge.

**DAVID** And then may be incredibly effective in reaching target levels of things, whatever those are. In terms of the technical approach to revascularization, I think we are continuing, from a percutaneous standpoint, we're making iterative changes by absorbable revascular-- vascular scaffolds are being tested. Whether they will truly make a huge difference is not clear. We're continuing to make the stents thinner with thinner struts and better in terms of being able to resist the compressive forces. But I think those are iterative changes. I don't think that as yet we see a home run.

**JAY WIDMER:** OK.

**DAVID** Maybe it's different with surgery.

**HOLMES:**

**LYLE JOYCE:** No, I agree. I think a lot of the advancements are going to be in the medical realm. From a surgical standpoint, particularly if there continues to be equipoise between the two technologies, I think maybe we will swing more towards some more hybrid approaches. You know probably the best treatment for any patient is an internal mammary down to the LAD. And then, maybe some of those other lesions will be, particularly if the technology improves even as well as it is and even more, those other lesions will be better treated in the cath lab. And then we can offer a truly minimally invasive approach, surgically, to get the important lesion taken care in the LAD and then finish it up in the cath lab.

**DAVID HOLMES:** Tell us about the future then, of a mammary artery that could be on the shelf using sort of biotech genetic engineering stuff that you could then in the operating room have the technical people bring you three mammary arteries and put them to every place and do it sort of as minimally invasive as that. Is that reality? Is that coming? Is it feasible? Do you think or look forward? Because that would be a true game changer.

**LYLE JOYCE:** Right. I think the best way to say that is, I think that is the future. My concern is, is it always going to be the future? We just-- I mean, we've tried so many ways to engineer artificial vessels and none of them have panned out as yet. But I think that is the direction that we need to go from a surgical standpoint. If we could do that, it would be so much better for the patient.

**DAVID** Terrific.

**HOLMES:**

**JAY WIDMER:** Great. Well Dr. Holmes, Dr. Joyce, thank you both so much for agreeing to do this. And thank you all for joining us here on the heart.org on Medscape for these very important insights.