

## Left Main Coronary Disease – Selecting the Best Treatment

Announcer: Welcome to the Mayo Clinic cardiovascular continuing medical education podcast. Join us each week to discuss the most pressing topics in cardiology and gain valuable insights that can be directly applied to your practice.

Dr. Klarich: Hi, my name is Kyle Klarich, and I'm Vice Chair for Clinical Practice in Cardiology, a consultant in Cardiology in Rochester, Minnesota at the Mayo Clinic, and we are here today for one of our sessions Interview with the Experts, and I'm joined by two of my colleagues, Dr. Juan Crestanello, Professor of Surgery and chair of the Department of Cardiovascular Surgery, and Malcolm Bell, Vice Chair of Cardiology and Professor of Medicine. And we are gonna take on the topic today of left main coronary artery disease, selecting the best therapy for your patient. And we're gonna start out because of the new, relatively new trial, the EXCEL trial that has raised our awareness and recent guidelines that were published. And maybe I'll just start out by asking Juan, what was the EXCEL trial? Can you give us a little summary of what kind of patients they studied, and what that major outcomes were?

Dr. Crestanello: Sure. Thank you, Kyle. So the EXCEL trial was prospective, multicenter, randomized trial that enrolled around 1900 patients with left main coronary artery disease, and those patients were randomized either to PCI or coronary artery bypass surgery. The primary outcome was a combined endpoint of death, stroke, or myocardial infarction. The trial followed patients to up to five years, and at five years, the primary outcome, death, stroke, or myocardial infarction was not different between coronary artery bypass surgery or percutaneous coronary intervention.

Dr. Klarich: Great, thank you. Do you think that the population of patients within the EXCEL trial was representative of what most of us see in day to day practice?

Dr. Crestanello: Well, the population was, as any clinical trial, was strictly defined. The severity of the coronary artery disease was what we call, or the complexity of the coronary artery disease was low or intermediate, and that was evaluated by the syntax score, which was overall low, and that tells you that the severity and complexity of coronary artery disease was low or intermediate. And in addition to that, there was a low proportion of a diabetic patients, a low proportion of diabetic patients on 30%, who are the patients who, in general, had more extensive coronary artery disease, and more complex coronary artery disease, and we know that those patients are the ones that benefit the most from surgical revascularization. In addition, there was a, the majority of the patients were male, and there was a low proportion of female patients in the trial.

Dr. Klarich: And was there, do you think there was any differences between the CABG patients and the PCI patients, or percutaneous intervention patients?

Dr. Crestanello: Well, there was some baselines difference, but one of the differences that it can be impactful in terms of the outcomes was the difference in the compliance of medications in the follow up period, where the the PCI patients were, that there was a higher proportion of patients who were taking antiplatelets, dual antiplatelet agency agents than in compared to the coronary artery bypass surgery patients.

Dr. Klarich: And what was the, or was there a time dependence on the outcomes?

Dr. Crestanello: Yeah, certainly there was a time. If you look at the overall result of the trial, the composite endpoint of death, stroke, or MI, there was a initial benefit for PCI, and about two and a half to three years, there was a change in the outcomes, where you could still see an increased rate of death, stroke, or MI on the PCI patients, compared to the CABGs. So after the first two and a half years, the initial advantage for of a PCI was lost, and that was mostly related to the increased rate of a myocardial infarction, and the increased rate of death after that two and a half years.

Dr. Klarich: That's really interesting. So there was an initial interest, or initial benefit to the PCI group, and then the curves crossed right in the middle of about two and a half years of the five years, and then there was the later timeframe, there was a benefit for the CABG patients, based on myocardial infarction and death, as opposed to stroke. So that's very interesting, not the composite endpoint then. What does the result then tell us about our clinical practice? How does that impact, and maybe I'll ask both of you to comment on what your, has this changed your practice at all, the EXCEL trial? How do we take this into account when we're thinking about an individual patient in the office? Malcolm, maybe I'll let you go first.

Dr. Bell: Thanks, Kyle. I think that it's just worth remembering that when you asked about your, the type of patients in this study, the first thing I think we need to be aware is that 15% or so were actually ACS patients. They'd had an MI in the last week or so, so that's a very small population, but it's a population we see a lot, obviously, in the hospital practice. About a 60% had stable ischemic heart disease. So this is really the group of patients that you're talking about that you're discussing the findings of their angiogram in the office. But I think that it probably hasn't changed our practice too much, because obviously, we've been doing bypass surgery on these patients for a long time, but we certainly here at Mayo and other places have been doing PCI for left main disease for many years. And remember, the original EXCEL trial publication was back in 2016, so, and that's really, I think, sort of shaped how we've approached these patients along with a couple of other large left main trials. But I think that it's important to remember that many patients were excluded from that trial, and so like any randomized trial, it's a selected population. So I think the important thing though is, and this is something that hasn't changed in our practice, except for an emergencies, we do not do ad hoc PCI in left main disease in stable patients. I think it's important to take them off the table, and have that discussion with them. And then it's just a matter of patient selection, and we can go into more detail in terms of that. But so, as I said, I think it hasn't really changed our practice here too much. We've got too very effective and safe procedures, but as Dr Crestanello pointed out, it's the long term outcome which is really important, and we did see those curves start to diverge. They may diverge even further in 10 years time with a 10 year follow up. This was a non-inferiority trial, and it still was non-inferior at five years, but you could see that reversal and separation of all those curves.

Dr. Klarich: So Juan, thank you, Malcolm. Juan, would you have anything to add to that? Has it changed the way you practice clinically?

Dr. Crestanello: Not really. I mean, I agree with the Dr. Bell. We here at Mayo, we had collaborative approach in terms of decision making, where we, the heart team has discussion about the patients, and based on the patient, overall patient situation, we make a decision what the best treatment would be. And that involves considerations in terms of the complexity of the left main disease, the presence of additional coronary artery disease in other territories, like the LADI territory, the circumflex of the right coronary artery, the overall cardiac function, the presence of other cardiac pathologies, and the age of the patients, the life expectancy, and other comorbidities, and the ability to pull the patient successfully through surgery, as well as the patient's preference are all factors that we consider in that type of decision.

Dr. Klarich: So then I'll pose this question to both of you too, is what are the patients that you would consider to be most benefited from coronary artery bypass? Which left main patients would you have a tendency to recommend coronary artery bypass grafting versus percutaneous coronary intervention?

Dr. Bell: Well, maybe as I'm the not wearing in the surgical hat, I think it'd be reasonable for me to give an honest opinion there, because as Dr. Crestanello says, we do work in concert together, and we are referring each other patients, and that's been a longstanding practice here at Mayo. But I think when you see patient who's got an angiogram that clearly shows severe left main disease, I think the patients that are best suited for surgery, and the ones that we would tend to sort of shy away from doing PCI on would be those who have distal left main, this is bifurcation, it's already more complex disease, but particularly if it's associated with multivessel disease, particularly complex coronary artery disease. And also, if we can't completely revascularize the patient, I mean, that's clearly an indication for surgery. And as Dr. Crestanello said, the diabetic patient, I mean, these are the patients that we probably should be doing bypass surgery on. I also think that, all things being equal, probably the younger patients, we probably really have to, perhaps, have a preference for recommending bypass surgery over stenting. And one thing which we haven't discussed is the mortality difference, and although that was not statistically significant, significantly different in the five year follow up, it did cause some controversy, about a 3% absolute difference, and we don't know what's gonna happen in the future. And so that younger patient, I think they really need to be appraised of the possible benefit in terms of needing further procedures, and particularly that there might be a survival difference. The older patient, though, these are very often the patients who come along with lots of comorbidities. Very often the surgeons are maybe a little hesitant about offering open heart surgery, and if they have suitable anatomy, and we can offer complete or near complete revascularization, I think those are the ones that are better for PCI. The easy ones, of course, are the ones that have ostio and shaft disease, and, but again, I think this comes down to a shared decision making with the patient. Dr. Crestanello also mentioned about patient preference, and sometimes you have a patient that you really think probably is gonna benefit from surgery, but, and you can show them survival curves, and all the data, but they're reluctant to undergo open heart surgery. It's a small number of patients, but I think we have to make sure we accommodate their expectations, and what they would like to have in terms of revascularization. Dr. Crestanello, did I miss out anything there? I mean, does that resonate with you?

Dr. Crestanello: Certainly, I think that, I agree with all those statement, and the only thing that I will add in terms of the young patients, and also the diabetic patients, the benefit, the long term

benefits of bypass surgery is enhanced by the use of arterial revascularization. So the adding a second coronary artery, in addition to the edema to LAD, that will have an additional advantage in terms of long term survival. One of the things that we learned from the EXCEL trial, and I think it's important to point out is that the mortality benefit of surgery, or the survival benefit of surgery are not seen until the two and a half years or so. That's the statistical, when the curve starts to cross and diverge, and that provides an important piece of information. If we have a patient who, for whatever reason, either because of their age, or because of the comorbidities, their life expectancy is gonna be limited less than two and a half years, the possibility of realizing the benefit from a coronary artery bypass surgery are gonna be very limited, and in those patients, PCI would be beneficial for them, rather than surgery.

Dr. Klarich: So if I can summarize, and please feel free to correct me if I say anything out of line here. I'm a non-invasive, nonsurgical colleague here, but all left main patients are not the same is what I'm hearing, and that, since they're not the same, we would probably have a tendency to lean towards coronary artery bypass grafting in younger patients with a longer survival, in patients with complex coronary artery disease, and maybe those that are, have less comorbidities, but also maybe lean towards it in diabetes, even though that might be a little counterintuitive, but we've learned that from many years ago. And then the PCI patients, maybe we would tend towards the percutaneous interventions, and those patients that have less lesion complexity, so the syntax score of less than 33, and increased comorbid problems, and a shorter lifespan. But at the end of the day, the heart team, and the discussion between the patient, the surgeon, and the cardiologist interventionalists are very important, and we have to take into the consideration the patient's expectations and wishes. And one last thing I think was important to point out is that you mentioned the option for arterial grafts, so left internal mammary, right internal mammary, maybe even both in some of these patients, and so that's a consideration to add to the list, even though it wasn't directly necessarily covered in their earlier discussion, so this is great. Well, it's been great to have this conversation, and I hope it helps our listeners to better understand how we think about these patients with what we consider to be a very serious illness that's left main coronary artery disease. Thank you for your attention. Until next time, have a great day.

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