Cath Lab Digest

A product, news & clinical update for the cardiac catheterization laboratory specialist

CATH LAB SPOTLIGHT

St. Luke's Monroe Interventional Radiology and Cardiac Cath Lab

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Tell us about your cath lab.

St. Luke's Monroe has a shared lab with a GE 3100 fluoroscopy system (GE Healthcare), which is used by interventional cardiology, interventional radiology (IR), vascular surgery, and occasionally, cardiac electrophysiology (EP). We also have one smaller swing lab with a portable C-arm. Plans are already underway to build out a second, fully functional state-of-the-art cath lab, although the project was delayed due to the pandemic. The plan is to expand within a 10,000 square-foot suite, inclusive of a state-of-the-art procedure room, nursing station, break/locker rooms, and patient holding bays.

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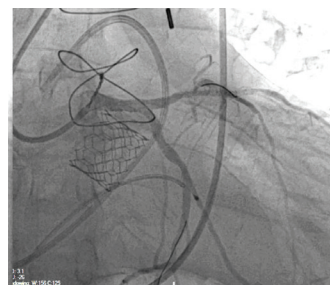
In This Issue

TAVR

Door-to-Valve Time of 120 Minutes for Severe Aortic Insufficiency and Cardiogenic Shock in ACS

Muhammad Umair Bakhsh, MD; Dalvir Gill, MD; Faraz Kazmi, MD; Immad Sadiq, MD; Talhat Azemi, MD



Severe aortic insufficiency in the setting of acute coronary syndrome (ACS) can manifest in cardiogenic shock requiring immediate intervention due to the progressive rise in the left ventricular end diastolic pressure (LVEDP) and hemodynamic instability. There is limited data demonstrating the safety of emergent valve-in-valve (ViV) transcatheter aortic valve replacement (TAVR) for patients presenting with decompensated aortic insufficiency of a failed aortic homograft in the setting of acute coronary syndrome. Our case demonstrates the feasibility of emergent TAVR combined with left main (LM) bifurcation percutaneous coronary intervention (PCI) within 2 hours of hospital presentation for ACS and chronic bioprosthetic aortic insufficiency of a failed homograft with no time for any preoperative planning.

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CALCIUM CORNER

Coronary Intravascular Lithotripsy (IVL):

Research Roundup at TCT With Drs. Dean Kereiakes, Ziad Ali, Akiko Maehara, and Yasin Hussain




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Coronary Intravascular Lithotripsy (IVL):

Research Roundup at TCT With Drs. Dean Kereiakes, Ziad Ali, Akiko Maehara, and Yasin Hussain

Consistency From 30 Days to One Year for Coronary IVL

Dean Kereiakes, MD

Following its presentation at TCT21 in a featured clinical research session, Disrupt CAD III co-principal investigator, Dean Kereiakes, MD, Medical Director of The Christ Hospital Heart and Vascular Center and the Christ Hospital Research Institute; Professor of Clinical Medicine, The Ohio State University, discussed the updated data since the primary 30-day outcomes were presented at TCT 2020.

What is the significance of the one-year follow-up data from the Disrupt CAD III study, which was included by TCT as one of the meeting's best abstracts in the featured clinical research session?

Dr. Kereiakes: It is very significant that the one-year data show a sustained and persistent relative benefit of IVL for lesion preparation prior to coronary stenting. This is the first robust one-year data presented on coronary IVL, which is very important, because there were concerns, as with the use of ablative technologies, that in late follow-up there might be some loss of the benefit as predicted by the minimal stent area (MSA) and percent stent expansion at the initial procedure. These were phenomenal levels from the optical coherence tomography (OCT) sub study — 102% stent expansion and MSA of 6.5 mm^2 at the site of maximum lesion calcification. Since we were able to achieve these excellent levels, one would predict, based on all other previous imaging studies, that there should be a low rate of target lesion revascularization (TLR) and stent thrombosis, which is exactly what we found.

Were there any other potential concerns that you had about the one-year outcomes?

Dr. Kereiakes: Some had expressed concerns that there might be a negative impact of the energy generated by IVL, similar to what we see with the friction induced by rotational and orbital atherectomy. The reassuring answer is that it does not look like there is any negative impact, as the data are great. When, at one year, you have an ischemia-driven (ID)-TLR of 4.3% and a total stent thrombosis rate of 1.1% with only one patient (0.3%) having a stent thrombosis beyond 30 days, that bodes very well.

Was there anything surprising about the data itself?

Dr. Kereiakes: No, I actually thought the data were predictable, based on the optimized stent implantation results we were able to achieve by pretreating these severely calcified lesions – 100% of which were classified as severely calcified, as adjudicated by an independent core lab.

Now that durable one-year outcomes have been shown, what is the next step from a clinical research perspective?

Dr. Kereiakes: The next step is to analyze the post-market approval study being done through the American College of Cardiology's CathPCI registry, which is very innovative. The analysis is going to be very helpful, as it will expand our observations around using IVL for lesion preparation in a much broader population of real-world patients.

Given that Disrupt CAD III was a single-arm study, how do you contextualize the results of the one-year findings?

Dr. Kereiakes: Without a randomized comparator, it is always challenging and difficult. Recall that we set up the best performance goals possible, using a similar population, definitions, and endpoints to ORBIT II, which was the pivotal trial for FDA approval of orbital atherectomy. This was probably the best designed, non-randomized comparator possible. That being said, although it remains a cross-trial, non-randomized comparison, when you look at the one year data, Disrupt CAD III shows a 13.8% major adverse cardiac event (MACE) rate and ORBIT II shows a 16.9% MACE rate. It is a very intriguing, hypothesis-generating, but non-randomized comparison.

For those physicians who may have been waiting for longer-term data to prove the effectiveness of IVL therapy, what would you tell them now that the one-year data is available?

Dr. Kereiakes: Of course, to look at the data, but also to look at the best data from the other sources of calcium modifying technologies — take in the totality of the data. That means peri-procedural results to 30 days and at one year. There has never been a cohort of patients with more severely calcified target lesions than those enrolled in Disrupt CAD III for U.S. FDA approval of coronary IVL. Consider the substrate that was enrolled and the peri-procedural outcomes, with zero perforations, zero abrupt closures, zero no re-flow with IVL alone and only one patient out of the entire series with an Ellis type 1 micro-perforation following stent deployment that sealed by itself. When I look at these data, we see a low complication rate and great outcomes at 30 days that now persist out to one year. Knowing these data, going forward, I would hesitate to approach severely calcified target lesions without IVL.

"We see a low complication rate and great outcomes at 30 days that now persist out to one year. Knowing these data, I would hesitate to approach severely calcified target lesions without IVL." — Dean Kereiakes, MD

Is there anything else that stood out to you about the IVL data presented at TCT?

Dr. Kereiakes: When you look at all of the IVL data, we have 47 sites in four countries with Disrupt CAD III and an additional pooled analysis of data from 72 sites in 12 countries. At all of these different sites across multiple continents and countries, there is remarkable consistency in the safety and effectiveness endpoints achieved. It reflects the ease of use of IVL. It is a balloon. Every interventionalist, I don't care what subspecialty you are, uses balloons. And that includes the relative safety of the technology as well. Delivering high technology in a primitive delivery system. It doesn't matter whether you are in Europe or the U.S. Doesn't matter if you are in a big center or little center. The beauty of this observation is the consistency of safety and effectiveness, and we found no differences with IVL. I call IVL the great equalizer.

Applying Shocks in Eccentric Versus Concentric Rocks

Ziad Ali, MD, DPhil

Following its presentation at TCT21 in a moderated poster session, Ziad Ali, MD, DPhil, Director of the DeMatteis Cardiovascular Institute and Investigational Interventional Cardiology at St. Francis Hospital & Heart Center, shared his thoughts on the implications of the concentric versus eccentric calcium analysis among those patients enrolled in the Disrupt CAD clinical program.

Why is eccentric calcium so challenging to modify?

Dr. Ali: Simple. It is hard to modify. Balloon-based modification leads to the creation of a dissection at the site of minimal resistance. That is the fibro-calcific interface, the place where the fibrous tissue meets the calcium. This dissection allows vessel expansion, but the calcium remains unmodified. After stenting the calcium protrudes back into towards the lumen, reducing the potential minimal stent area. With atherectomy, the wire and thus burr must be biased into the calcium. If it is not, there is no chance of lesion modification. With IVL, most of the energy is lost into the soft tissue. So if there is only 90 degrees of calcification, i.e., 25% of the vessel circumference, 75% of the energy is dissipated. More specifically, the maximum energy in IVL is immediately perpendicular to the electrode.

Why is the Disrupt CAD OCT pooled analysis important for current clinical practice?

Dr. Ali: There is power in numbers. These data show categorically that the predominant mechanism of IVL is calcium fracture, and that the more the calcium, the greater the fracture. The ability of IVL to create luminal gain in severe calcification is unquestionable. Overall, the mean stent expansion and stent expansion at the site of max calcium was greater than 100%. The fact that the minimal lumen area was never at the site of maximum calcification is proof in and of itself.

What were the findings in the OCT analysis in concentric and eccentric lesions?

Dr. Ali: Fractures are much less common in eccentric rather than concentric lesions. But that's okay; you need fewer fractures in eccentric calcium because the rest of the artery is conformable. In general, lesion modification for an eccentric calcified lesion is unnecessary, unless it is a calcified nodule. That being said, within a heavily calcified segment of vessel, there will be multiple morphologies along the length of that lesion. Some concentric, some eccentric. IVL helps all the way along the length by creating lots of fractures at the more concentric sites and fewer fractures, because fewer are needed, at the eccentric sites. The take-home message is that even in eccentric lesions, there was a consistent improvement in stent expansion and luminal gain compared to concentric lesions. So IVL liberates vascular compliance through calcium fracture appropriate to need.

How do these outcomes compare to what you see in the clinic?

Dr. Ali: We are definitely still learning, but the clinical experience is very similar to the trial results. Not surprisingly, there was tremendous consistency in terms of safety and efficacy among all of Disrupt CAD studies, so we wouldn't expect that to be different in the real world. At St. Francis, we have done over 100 commercial cases and one of our more noticeable findings is how well tolerated IVL is in the very high-risk patient, such as those with very low ejection fraction, high end-diastolic pressure, severe pulmonary arterial hypertension, and multivessel disease. We don't see the same hemodynamic fluctuations that we sometimes see with other lesion prep strategies.

"One of our more noticeable findings is how well tolerated IVL is in the very high-risk patient, such as those with very low ejection fraction, high end-diastolic pressure, severe pulmonary arterial hypertension, and multivessel disease." — Ziad Ali, MD, DPhil

Are there any coronary IVL best practices that will help interventionalists achieve similar results to what was reported?

Dr. Ali: Image, image, image. Intravascular imaging determines the severity and distribution of calcium. Using the St. Francis Calcium Scores can help determine whether or not you even need advanced lesion prep. By OCT, if the calcium is 5 mm long, 0.5 mm thick and 50% of the arc, advanced prep is necessary. By intravascular ultrasound (IVUS), if the calcium is circumferential, 270 degrees for 5 mm, <3.5 mm at the site of calcification, and calcified nodule, advanced prep is necessary. Remember, the more the rock, the better the shock!

Cracking the Nodular Code

Akiko Maehara, MD

Dr. Maehara shares her thoughts regarding the Disrupt CAD Pooled OCT Calcific Nodules Analysis presented at TCT21.

How do you define a calcific nodule and what makes these nodules so difficult to modify?

Dr. Maehara: As defined by OCT, the eruptive calcific nodule is accumulation of small calcium fragments underlying the calcified plaque typically protruding the lumen. Nodular calcium[1] (healed calcified nodule, i.e., calcified nodule with thick, fibrous cap) is probably more difficult to modify, because calcium is hard structured and because nodules protrude into the lumen, which makes fracturing them very difficult with suboptimal stent expansion.

Why is the Disrupt CAD OCT analysis of calcified nodules relevant to today's practice?

Dr. Maehara: This analysis is relevant because lesions with calcified nodules present with poor long-term outcomes, even with a good MSA at index procedure. There is a very robust recent Japanese article[2] published in *Atherosclerosis* showing that when we compare severe calcified lesions with or without calcified nodules, the lesions with calcified nodules have poor outcomes compared with lesions without calcified nodules. While MSA is the most important factor to predict future events, long-term outcomes are still poor in the presence of calcified nodules, regardless of the index MSA. In another Japanese publication using the in-stent restenosis (ISR) captured by directional coronary atherectomy[3], when they studied the ISR cases, the lesions with calcified nodule showed nodules protruding through the stent struts, and the calcified nodule was pushed out. This is not something we have seen before, and we are still learning about it.

What did we learn from this study on the impact of coronary IVL on nodular calcium?

Dr. Maehara: The nodular analysis is still a preliminary finding, as it is looking at procedural results, so we should acknowledge that we need longer-term clinical follow-up of these patients. That said, my sense looking at this OCT analysis and considering my experience with nodular lesions treated without IVL, is that IVL is disrupting the calcified fragments that are bonded together to create the calcific nodule. IVL seems to be reshaping the calcified nodule, which might mean more symmetric stent expansion and less protruding calcium through the struts during follow-up, and this theoretically may lead to better long-term outcomes than treatments with other calcium modification therapies. We really have to see clinically good outcomes in the IVL cohort compared to a non-IVL cohort, or possibly look into the OCT again in the chronic stage to see if the nodules are protruding inside the stent. These are the kind of data needed to support this hypothesis, and will come with longer follow-up.

How would you explain IVL's ability to successfully modify nodules, as shown in this analysis, to the interventional cardiologist who does not consider the technology a great tool for this particular calcium morphology?

Dr. Maehara: We all know these cohorts have very poor outcomes, even in comparison to severely calcified lesions without nodules. While the calcified nodule looks like a calcium rock, pathologically, the very dense calcium is small calcium fragments connected with fibrous tissue. As such, the IVL acoustic energy can disrupt the small fragments, affecting the calcified nodule. Balloons, on the other hand, are subject to wire bias and are not

"While the calcified nodule looks like a calcium rock, pathologically, the very dense calcium is small calcium fragments connected with fibrous tissue. As such, the IVL acoustic energy can disrupt the small fragments, affecting the calcified nodule." — Akiko Maehara, MD

changing the shape of the calcified nodule. Ablation therapies are polishing only one side of the nodule, just 15% of it.[4] To be able to ablate more of the nodule with atherectomy, say 50%, you would have to ablate multiple times, which we typically can't do. This is why IVL disrupts calcified nodules with much greater ease than other calcium modification modalities.

Given that these are acute procedural outcomes, what is important to look at next with coronary IVL in calcific nodules from a research perspective?

Dr. Maehara: We have to see clinical outcomes in the long term. No matter how good stent expansion is, these lesions have poor outcomes, because of protruding nodules. Will fracturing the calcified nodule help the long-term outcome? Will the acute appearance correlate with the outcomes? We will see over time. In addition, we need to better understand different types of calcified nodules and what the optimal outcomes are for each type of nodule, along with the ideal calcium treatment device for each type. It is also important to study patients undergoing hemodialysis, as they are more likely to have accumulation of calcification, and as a result, more calcified nodules. They are truly a unique cohort with very poor outcomes. This is even more critical to consider in international regions where transplants are not an option.

References

1. Torii S, Sato Y, Otsuka F, et al. Eruptive calcified nodules as a potential mechanism of acute coronary thrombosis and sudden death. *J Am Coll Cardiol.* 2021 Apr 6; 77(13): 1599-1611. doi: 10.1016/j.jacc.2021.02.016
2. Sugane H, Kataoka Y, Otsuka F, et al. Cardiac outcomes in patients with acute coronary syndrome attributable to calcified nodule. *Atherosclerosis.* 2021 Feb; 318: 70-75. doi: 10.1016/j.atherosclerosis.2020.11.005
3. Yamamoto MH, Maehara A, Kim SS, et al. Effect of orbital atherectomy in calcified coronary artery lesions as assessed by optical coherence tomography. *Catheter Cardiovasc Interv*. 2019 Jun 1; 93(7): 1211-1218. doi: 10.1002/ccd.27902
4. Nakamura N, Torii S, Tsuchiya H, et al. Formation of calcified nodule as a cause of early in-stent restenosis in patients undergoing dialysis. *J Am Heart Assoc.* 2020 Oct 20; 9(19): e016595. doi: 10.1161/JAHA.120.016595

Gender Equality in Treating Calcium

Yasin Hussain, MD

Dr. Hussain discusses the Disrupt CAD Pooled OCT Female vs Male Analysis at TCT21.

What do we know about gender analyses from large, previously conducted percutaneous coronary intervention (PCI) studies?

Dr. Hussain: In general, moderately to severely calcified lesions are associated with higher rates of target lesion failure, myocardial infarction, stent thrombosis, and cardiac death, both in hospital and long-term, and independently predict ischemia-driven revascularization in both men and women. Typically, women undergoing PCI have more comorbidities and worse periprocedural complications. When it comes to PCI of severely calcified lesions, women have as much as a 2-fold higher risk of coronary perforations and a 5-fold higher risk of tamponade compared with men, and the risk of in-hospital mortality is reported to be 20% higher compared to men.

From your perspective, what were the key takeaways from this analysis?

Dr. Hussain: This pooled analysis of the Disrupt CAD trials is the largest to evaluate the use of IVL to treat severely calcified coronary lesions. The key findings were, first, that IVL is safe and effective in both men and women. Second, we found that IVL treatment of severe calcification resulted in the lowest observed rates of procedural complications in both men and women compared to other atheroablative options.

What is the impact of the gender analysis of the Disrupt CAD Pooled Studies on current practice in both male and female patient populations?

Dr. Hussain: IVL appears to be the great equalizer of outcomes between men and women, showing, for the first time, lower procedural complications in women compared to men. IVL should be considered first-line treatment for severely calcified lesions, especially in women, given their increased risk of severe procedural complications and the poor associated clinical outcomes, including heightened mortality risk.

How do outcomes from the Disrupt CAD pooled gender analysis compare to previous gender studies conducted with calcium modification tools?

Dr. Hussain: Several small studies have looked at the differences in outcomes using rotational atherectomy and orbital atherectomy based on sex. Atheroablative devices demonstrate a 2- to 5-fold higher rate of periprocedural complication in women compared with men. IVL, in our study, shows low complications and similar results in men and women. However, it is important to highlight that this observation is based on a small, non-randomized series and will require additional confirmation.

What should interventional cardiologists expect to learn next about coronary IVL in females — where should the research take us?

Dr. Hussain: Future studies should compare the safety and efficacy in a randomized manner, with IVL versus a standard atheroablative treatment strategy, in order to confirm and understand the generalizability of our preliminary results. ■

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