AN INTERVIEW WITH...

Binita Shah, MD, MS, FACC, FSCAI

Dr. Shah discusses the benefit of colchicine in cardiovascular disease, the role of diet after coronary intervention, DEI efforts in interventional cardiology, and more.

Your research in recent years has been dedicated to anti-inflammatory therapies for cardiovascular disease, with several papers and trials specifically focusing on the role of colchicine. How would you summarize what we currently know regarding the benefit of colchicine in cardiovascular disease?

Thanks to pioneers in the field like Drs. Peter Libby and Paul Ridker, we now know that inflammation plays an independent role in the development of cardiovascular disease and adverse cardiovascular events and that targeting this inflammatory pathway lowers the rate of major adverse cardiovascular events. Our group at New York University School of Medicine was the first to show that patients with gout treated with colchicine had a lower rate of myocardial infarction (MI).[1] We also showed that in patients with gout and without kidney disease, the use of colchicine was associated with a decreased risk of developing coronary artery disease.[2]

Our group dug into the potential pathophysiologic mechanism of benefit and demonstrated that colchicine affects selectin molecules on neutrophils, thus decreasing the adherence of activated neutrophils to inflamed or injured endothelium, thereby decreasing further activation of the neutrophil inflammasome and production of IL-6 (a precursor of C-reactive protein [CRP]).[3] We also showed that clinically used doses of colchicine inhibit the interaction between neutrophils and platelets but not platelet-to-platelet aggregation, thus targeting activated platelets at the areas of inflammation without an increased risk of bleeding.[4]

Since then, both Dr. Stefan Nidorf and Dr. Jean-Claude Tardif conducted large, randomized, placebo-controlled trials showing a reduction in major adverse cardiovascular events in patients with stable coronary artery disease (LoDoCo2) and recent MI (COLCOT), respectively. Our ongoing CLEAR SYNERGY trial (with Study Chair Dr. Sanjit Jolly) will be the largest randomized trial evaluating the benefit of colchicine in patients with recent large MI.

You are Principal Investigator for the currently enrolling neutrophil substudy of the CLEAR SYNERGY trial. What are the main questions you plan to answer with this trial? And, what impact might the results have on patient care?

Our National Institutes of Health (NIH)–funded neutrophil substudy of the CLEAR SYNERGY trial aims to evaluate how colchicine (versus placebo) affects different stages in the pathophysiologic role of neutrophils in acute MI to get a better understanding of the potential mechanism of benefit in this population. We also plan to evaluate the genome, as there are some polymorphisms linked with colchicine resistance. Together, we hope to use clinical parameters, biomarkers, and DNA to determine which patients would benefit from the addition of colchicine to their cardiovascular regimen and which patients would not. As we move toward precision medicine, it is important to create these types of profiles so we can ultimately personalize a patient's medical therapy.

What is next with your research that you are most excited about?

Our Veterans Affairs (VA) Office of Research and Development–funded randomized COLCHICINE-PCI trial was the first to show that if given before an inflammatory-triggering insult, colchicine can dampen the rise of IL-6 and CRP.[5] We used these data as the basis for our international COLCORONA trial, for which I obtained NIH funding as the United States lead. The idea was that, if taken early in the COVID-19 diagnosis, colchicine could dampen the inflammatory response, and we did show a lower rate of hospitalization due to COVID-19 when compared with placebo.[6] Although we cannot usually predict when a patient will have a spontaneous MI, we know that patients with prior coronary revascularization undergoing intermediate- or high-risk noncardiac surgery are at risk of postoperative myocardial injury and other adverse cardiovascular events. I recently obtained funding from the VA Office of Research and Development to run a multicenter ran-

(Continued on page 72)

(Continued from page 74)
domized, placebo-controlled study (POPCORN) to evaluate the effects of perioperative colchicine in this cohort and are excited to launch recruitment in a few months!

As someone who specializes in radial artery catheterization, can you speculate how the role of radial access for cardiac intervention may evolve in the coming years? Are there any particular breakthroughs you hope to see?

Over the last decade, we have seen a lot of advancement in the tools available to safely and easily perform invasive coronary angiography and percutaneous coronary intervention (PCI) via radial artery access. We've also seen the proportion of radial cases in the United States rise from 10% to > 40% nationally. We've conducted a few single-center studies in the past that allowed us to better understand the association between experience and access site crossover rate, the effect of left versus right radial artery access on radiation exposure in patients at high risk for failure via right radial artery access, and which patients would benefit from a universal catheter via the radial artery approach versus a dedicated two-catheter technique. I believe that all of these studies have allowed us to keep moving forward as we optimize the procedure and increase our rate of procedural success via radial artery access (our group uses the radial artery in > 95% of cases) while minimizing an increase in procedure time and radiation exposure. I hope that the field continuously evolves so that operator radiation exposure is limited across the board and the proportion of radial cases in the United States continues to rise.

You and colleagues published the EVADE-CAD dietary intervention trial, for which you were Principal Investigator.[7] What are the areas for further research regarding diet and coronary artery disease? When it comes to discussing diet with your patients, what have you found to be successful?

Our outcomes after coronary stents are only as good as the medical and lifestyle therapy that go along with an optimized technical procedure. Our patients often ask us after a procedure, "What next, doc? What do I need to change with my diet?"

Previous diet studies were riddled with confounders; a holistic approach to diet, exercise, and stress reduction would be compared to essentially a bag of potato chips and without background statin therapy. In the EVADE-CAD study, we took patients who underwent recent PCI and were on optimally tolerated guideline-directed medical therapy and randomized them to 8 weeks of the American Heart Association (AHA) diet or the plant-based vegan diet. We kept both intervention arms as similar as possible; we provided groceries and cookbooks/recipes that adhered to the spirit of the treatment arm, with the sole difference of animal-based protein replaced with plant-based protein for the vegan group. The study showed significant reductions in CRP and low-density lipoprotein levels with plant-based protein versus animal-based protein on a background of statin therapy. However, long-term follow-up showed that although patients made long-term changes to their diet based on trial participation, the majority were no longer adherent to whichever diet they were randomized to.[8] Of note, portion control of animal-based protein in the AHA diet arm was a source of difficulty for participants.

I now tell my patients who are coming in with recurrent events, despite their low-density lipoprotein at goal and tobacco cessation, that we may try the addition of colchicine; but, they will also need to increase the amount of plant-based food in their diet. Every patient is different—some do better with an all-or-nothing technique, and some do better with small changes. It's up to us to work with the patient to figure out what will work best for them over the long term.

Throughout 2022, you joined the Society for Cardiovascular Angiography & Interventions (SCAI) in efforts to promote the interventional cardiology (IC) fellowship match, and it was recently announced that IC will officially join the Match in 2025. Why was this something you wanted to support? How will this shift impact the next generation of interventional cardiologists?

This effort was a long time coming. Our fellows were being inundated with exploding offers and largely forced to make a decision about what they wanted to do very early in the course of the general fellowship, before they had time to really figure out where their passions truly lie. I'm grateful to SCAI (led by Drs. Doug Drachman, J. Dawn Abbott, Ajay Kirtane, and others) for getting this done. It was the right thing to do for our future fellows and colleagues. Now, they can take their time to figure out if IC is for them and weigh all their options after interviewing with as many programs as they would like.

As Co-Chair of SCAI's Diversity, Equity, and Inclusion (DEI) Taskforce, can you share the Taskforce's initiatives for 2023? How does your prioritization of DEI efforts inform your work as a clinical investigator?

We need to do better with representation of our patients in clinical trials because the data can only really apply to those similar to the participants in the studies. To increase representation, we must rethink how we design trials and consider and budget for community-based partnerships, diversity in trial leadership, and establishment of DEI committees to assess the impact of these efforts on trial recruitment. The SCAI DEI Taskforce is working with the IC community, industry partners, and the FDA to tackle these important issues.

Elsewhere in this issue, we've focused on women's heart health, but also important are the issues facing women cardiologists/interventional cardiologists, which is something you are passionate about. When considering the state of women in cardiology 10 years from now, what do you hope has changed?

I hope that it is no longer so difficult to be a woman in IC, battling microaggressions and unconscious biases and balancing work/family. I see that happening through increased representation, the growing number of male allies, and a shift in our society to emphasize the importance of work-life balance and self-care for all physicians.

What is one piece of advice you wish you had been given during your training years?

I received some great advice during my training, but I do wish I had heard earlier in training how others had struggled along the way, both clinically and with respect to research. Few people have had everything just handed to them with success on the first try; hearing about the failures with the successes, as well as learning how they wished they handled difficult interactions differently, is incredibly important to remind you that the rejections and "failures" are common. It's not just you. I can say that I had to send out many grant applications before I was awarded my first grant, and every application got easier after that. I didn't build this career overnight—it took years to slowly build up my clinical skills, research portfolio, and leadership roles. The most important thing was that I was following my passions, and I was doing something I truly enjoyed. ■

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Binita Shah, MD, MS, FACC, FSCAI
Associate Professor of Medicine
Director, Department of Medicine Clinical Investigator Track
Associate Director of Research, Cardiac Catheterization Laboratory
Leon H. Charney Division of Cardiology, Interventional Cardiology
New York University School of Medicine
SCAI Board of Trustees
Associate Editor, *Circulation: Cardiovascular Interventions*
New York, New York
binita.shah@nyumc.org
@BinitaShahMD
Disclosures: Advisory board for Philips Volcano; consultant to Terumo Medical.