A
fter 2 years of virtual sessions, the American Heart Association's flagship meeting returned to an in-person format in Chicago this November—with livestreamed offerings, of course. JAMA spoke with Scientific Sessions conference chair Manesh Patel, MD, who is the Richard S. Stack Distinguished Professor and chief of cardiology at Duke University School of Medicine. The following is an edited version of the conversation, in which the physician discussed late-breaking research and other timely topics from the meeting.

JAMA: I’d like to start with some COVID-related research. Several studies at this year’s conference dealt with the ripple effects of the pandemic on heart health. What did the data show, now that we’re approaching 3 years in?

DR PATEL: From 2010 to 2019, using a CDC [US Centers for Disease Control and Prevention] database looking at death certificates, we’d seen that cardiovascular mortality was slowly coming down and had dropped over those 9 to 10 years by about 9% or 10%. When COVID hit, we actually saw the cardiovascular event rates and mortalities going up. In fact, in 2020 the cardiovascular death rate went up by 4.1%. That represented losing about 5 years of progress that we’d been making.

At Scientific Sessions we had an opening session with the FDA [US Food and Drug Administration] Director Dr Robert Califf, the US Surgeons General Jerome Adams and Regina Benjamin, from both the Trump and the Obama administrations, the World Heart Federation President Fausto Pinto, and our American Heart Association President Michelle Albert. Dr Califf highlighted that this loss in lifespan and this disability has made us, unfortunately, one of the countries in the world where our health care and our outcomes are much worse than others at a cost level that’s higher. So we certainly have to work on how to keep our health care going the other direction from where we are now.

JAMA: Were there any other data around that? JAMA published a paper related to COVID-19 and STEMs.

DR PATEL: STEMs, or ST-elevation myocardial infarctions, are when people have chest pain. We try to get an EKG [electrocardiogram] in transport. If that EKG is showing you’re having a heart attack, we activate the team before you get to the emergency department and then sometimes you don’t have to check in. We just bypass you straight to the cath [catheterization] lab so we can take a look at your heart arteries to see if we can open them up. The goal being that the time from you calling to getting the artery open is 90 minutes.

We know that this time is really important. Investigators looked at over 114,000 patients in a cross-sectional national registry who had a heart attack during 2018 to 2021. There was unfortunately a statistically significant increase in time [to treatment]. And in those quartiles where the time went up the highest, we saw in-hospital mortality start to spike.

As an interventional cardiologist, I remember it was really complicated for us in the middle of the pandemic. We were saying, “Stay home unless you’re really sick. Oh, but you might be having a heart attack, so we need you to come to the health system.” And then in the health system, we were all taking time to learn how to put on PPE [personal protective equipment] and to put the patient in the room as fast as possible. So there were both inherent delays in the system and then delays as we tried to figure out how to take care of patients.

This study reaffirmed for us that guideline-directed care of opening the artery works. Even before COVID, on average people would sit at home with symptoms for 120 minutes. We know that over 20 years, we haven’t changed the 2-hour time period people sit at home. And so that time needs to shorten. What we also saw in this paper is that the [increased] time from when EMS [emergency medical systems] was picking the person up led to some of this increase in outcomes from heart attacks.

JAMA: Let’s talk about lipids. Researchers announced some surprising findings about triglyceride lowering. Tell us about that.

DR PATEL: I’ll just remind everyone that we’re going through a revolution of atherothrombosis. Atherosclerosis is an inflammatory atherothrombotic disorder. And the reason I’m using those words is because we have therapies aimed at different parts of that. There are a lot of agents used to reduce the athero component, there are some agents coming for the inflammatory component, and there are things like antiplatelets and other drugs we use for the thrombotic component. In the lipid space, for years we’ve used a lot of statins, but people will come in with a normal LDL [low-density lipoprotein] on statins and still have a heart attack. So what can
we do for those patients that still have what we call residual risk?

In that background, a new fibrate, pemafibrate, was studied in a large, randomized trial [the Pemafibrate to Reduce Cardiovascular Outcomes by Reducing Triglycerides in Patients with Diabetes (PROMINENT) trial] to see if it could reduce triglycerides. It also had a mechanism to maybe increase HDL [high-density lipoprotein] and see if that reduced cardiovascular events. In this several thousand–patient randomized blinded study, the agent did in fact reduce triglycerides by 25% but unfortunately had no change on major adverse cardiovascular events.

Going in, we knew that triglycerides are associated with risk, but we also knew that prior to this fibrate trial, 2 other randomized trials of fibrates had not shown any cardiovascular benefit compared to placebo. So now we have 3 trials with fibrates that aren’t different. Not to suggest you shouldn’t be on fibrates sometimes if your triglycerides are very high; there are clinical indications for it. But if you’re doing it in the moderate triglyceride range to reduce your cardiovascular risk, we have 3 trials that have shown it doesn’t change it. Yet fibrates are the second most prescribed medication, after statins, for lipid therapy. So I do think this study was very informing of practice.

JAMA: And the study was conducted among people with diabetes.

DR PATEL: You could have said the 2 [previous] trials were not as effective because [their populations] were not as high risk as you needed. So you try to take the high-risk patients—diabetics with high triglycerides. But it didn’t change risk.

JAMA: It reminds me of the studies that have not shown a benefit of increasing HDL.

DR PATEL: [High] triglycerides are certainly associated with adverse outcomes, or low HDL is. But therapies that are trying to change those numbers have not traditionally shown a benefit. Niacin is something that people think about and have used but that has not shown a difference.

There is an agent called icosapent ethyl that in randomized trials was shown to reduce cardiovascular events. People have often said, “Well that trial had a mineral oil comparator. So is that really true?” And it’s expensive; it’s very high-dose EPA [eicosapentaenoic acid]—it’s not fish oil. At this year’s sessions, there was another study, from Japan, looking at 1800 mg [of EPA], like the JELIS [Japan EPA Lipid Intervention Study]. This study [the Randomized Trial for Evaluating the Secondary Prevention Efficacy of Combination Therapy (RESPECT-EPA)] showed us that the moderate dose of EPA got really close to reducing clinical events. The P value was .055, but it was a really strong trend. My clinical impression is that it means that EPA at high dose is the agent that likely is going to reduce cardiovascular events. Importantly they found it didn’t change triglycerides that much, but it reduced cardiovascular events.

JAMA: There was also a trial of a small interfering RNA to reduce lipoprotein[a] [Lp(a)].

DR PATEL: We’ve talked about LDL, triglycerides, and HDL. Historically we haven’t tested—although it’s growing now—Lp(a), which is potentially the most atherothrombotic component of the lipid molecule or groups of molecules that we have. It’s a large atherothrombotic component that we can measure. If it’s elevated, we know it carries extended risk. We haven’t had therapies for it.

However, now we have these very specific small interfering RNA therapies that actually prevent Lp(a) from being produced. They don’t do it forever; you have to get the therapy at certain intervals. A phase 2 study called OCEAN(a)-DOSE [Olapasiran Trials of Cardiovascular Events and Lipoprotein(a) Reduction–Dose Finding Study] was presented at this meeting and simultaneously also published. Importantly, it showed that near 95% of that Lp(a) was reduced. So just like with the triglycerides story, we’ve now shown that something does change that molecule marker. Can we then go show that it reduces cardiovascular outcomes? We’re hopeful it will, and large trials are underway.

JAMA: Let’s turn to diuretics. There were 2 major trials presented at the conference that compared diuretics for heart failure and hypertension. What did we learn?

DR PATEL: This was another exciting part of the conference because these are extremely common questions. Let’s think about the TRANSFORM-HF [Torsemide Comparison with Furosemide for Management of Heart Failure] trial. A lot of patients with heart failure get more edema in their abdomen and sometimes have problems absorbing furosemide, or Lasix. A lot of clinicians who have heart failure patients keeping fluid in their abdomen will say we should...
switch them from furosemide to torsemide because it has better absorption. But it’s never been studied head-to-head. The investigator group did a randomized trial in about 2800 patients looking at total mortality and hospitalizations, and there was no difference. The message for me is that if your patient’s getting congested, you probably need to go to something else or increase the dose of the diuretic.

Another really innovative study looking at a very common question in hypertension was the DCP [Diuretic Comparison Project] trial. That was chlorthalidone compared to hydrochlorothiazide, and this was carried out solely in the VAs [Veterans Affairs]. All the patients, about 13,000, were on hydrochlorothiazide for hypertension.

Studies have previously shown that chlorthalidone probably has a little bit more potency and maybe 3 to 5 mm more of an effect on blood pressure compared to hydrochlorothiazide. I was surprised that they were similar [in the new trial]. The blood pressures were pretty similar, and the outcomes were exactly similar. The other lesson in there is that patients want the least [amount] of the medicine and docs don’t like to escalate or titrate up. But the guidelines say to titrate up.

**JAMA:** I was also struck by some research around gene editing.

**DR PATEL:** There was a late breaking science session on CRISPR [clustered regularly interspaced palindromic repeats] Cas9 [CRISPR-associated protein 9] technology that Jennifer Doudna won the Nobel Prize for several years ago. That technology was used to try to see if we could do something for transthyretin amyloidosis with cardiomyopathy. It showed that the infusion of the gene editing agent totally reduced production of the [transthyretin (TTR)] protein. Finding out if that will work in the long-term in those patients and what that life course is like is going to be a challenge. But it’s going to be a really important challenge because, at least in cardiology, we don’t usually have therapies that could potentially eradicate a disease.

**JAMA:** There were, similarly, really striking findings in a preclinical study of CRISPR base editing for PCSK9.

**DR PATEL:** The company’s product that they’re calling VERVE:101 is a CRISPR-Cas9-based therapy to try to target PCSK9, which is a very important pathway for how we handle LDL. They did the study in nonhuman primates. That’s important because now we’re in primates, not just mouse models. And that led to 83% lower PCSK9 protein and 69% lower LDL cholesterol with durable effects out to 476 days following dosing. These results are helping them initiate and support their first-in-human clinical trial.

**JAMA:** What did we learn at this year’s conference about cardiovascular effects of e-cigarette use or vaping?

**DR PATEL:** Unfortunately, we’ve known for some time that people who vape have fairly worrisome cardiovascular changes. Two analyses compared cardiovascular function among people who vape, people who smoke, and people who have not used either form of nicotine. And they found significant evidence of abnormal cardiovascular function in patients who smoked or vaped.

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Note: Source references are available through embedded hyperlinks in the article text online.