Medical News & Perspectives

Highlights From the American Heart Association's Scientific Sessions—ApoB as a Risk Marker, an Oral PCSK9 Inhibitor, and Aspirin and Dementia

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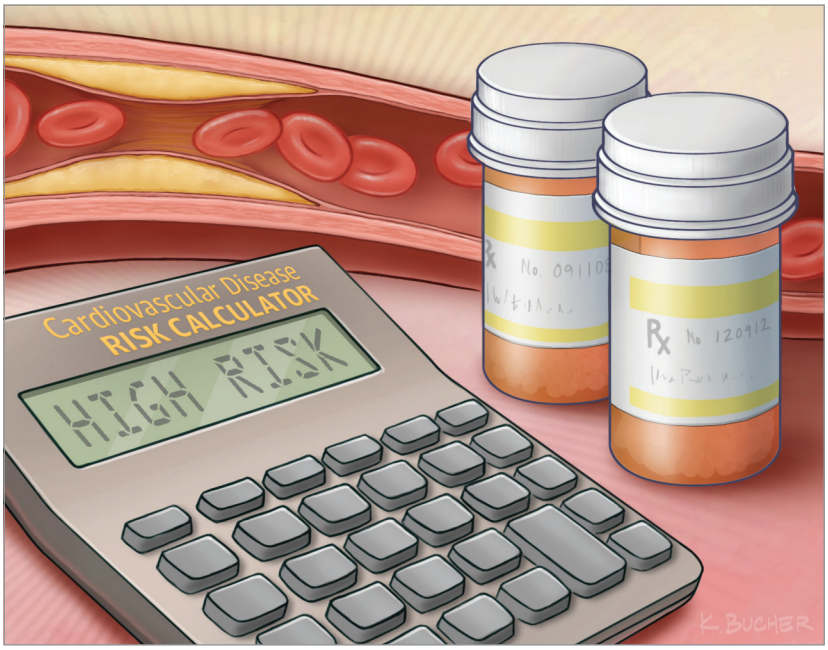
For the second year in a row, the American Heart Association's flagship scientific meeting took place virtually this past November. Just after it wrapped, *JAMA* caught up with conference chair Manesh Patel, MD, who also is the Richard S. Stack, MD, Distinguished Professor and chief of cardiology and clinical pharmacology at Duke University School of Medicine. "The science is always the show at the Scientific Sessions, and most of what we hope to do is to put it in context and allow people to interact with it so that hopefully they can put it into practice," Patel said in an interview.

Multimedia

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: Let's start first with a study simultaneously published in *JAMA Cardiology* about apolipoprotein B (apoB) and the risk of myocardial infarction (MI) in individuals with and without atherosclerosis. Can you tell us what this study found?

DR PATEL: The authors of this analysis looked at both the UK Biobank, a large prospective cohort with publicly available data, and at pooled data from 2 clinical trials—the FOURIER [Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk] trial of the [proprotein convertase subtilisin/kexin type 9] PCSK9-inhibitor [evolocumab] and the IMPROVE-IT [Improved Reduction of Outcomes: Vytorin Efficacy International Trial] trial of ezetimibe, another drug that can reduce cholesterol. The UK Biobank population is some 389 000 patients and the 2 trials had some 40 000 patients.

The authors looked at the apolipoprotein B concentration and total cholesterol, LDL-C [low-density lipoprotein cholesterol], non-HDL [non–high-density lipoprotein], and triglycerides. What they tried to do is to say, "Which of these parameters predicts the risk of future MI?" What they found was that apoB was the most predictive, both for primary and secondary prevention.

We traditionally haven't used apoB in clinical practice probably because we haven't had therapies that push that measure itself down, although some might be coming. I think this was the key finding to start to get our clinicians ready for therapies and predictors tied to apoB.

JAMA: Studies were presented on a novel PCSK9 inhibitor that is administered orally. This would be the first oral PCSK9 inhibitor. Tell us about that.

DR PATEL: There are 3 injectable PCSK9 inhibitors showing 50% to 60% reduction of LDL-C, with some concomitant cardiovascular risk reduction. And there are more coming that are longer acting, but they're injectables.

We saw data from Merck, which has an [oral] compound called MK-0616. They tested multiple doses and were able to show that patients had a reduction in their LDL-C that was on top of statins. And they had some broader data showing that they could reduce [healthy] patients' cholesterol [even] more. There was a little bit of variability depending on when participants ate. There was 20% less effectiveness if it was [taken] really close to eating. Some things like that that have to be worked out, but these data are exciting in that there's another potential option and it's not injectable. They still have to carry out the large trials, but it's exciting, nonetheless. It was pretty well-tolerated, also.

JAMA: Would an oral PCSK9 inhibitor be cheaper than an injectable? We know that's been a barrier.

DR PATEL: Great question. At the scientific briefing, the presenters could not tell us about the cost of it, and we don't know the cost. Obviously, we envision hopefully that it's cheaper and that it has the same effect. I hope and suspect it could be cheaper.

JAMA: Let's move onto a much cheaper drug—aspirin. In a secondary analysis of the ASCEND (A Study of Cardiovascular Events in Diabetes) trial, researchers looked at

the effects of aspirin on dementia and cognitive impairment. Can you tell us what they found?

DR PATEL: The ASCEND trial helped us understand that, for primary prevention, aspirin may not be as beneficial as we thought. It included people older than 40 years with any diabetes and no prior cardiovascular disease—so pretty broad inclusion criteria. Fifteen thousand patients in the United Kingdom were given 100 mg of aspirin daily, which is the worldwide dose, or placebo. They were followed for 7.4 years and then a year or so after the trial.

The study had both broad and narrow dementia outcomes. [This analysis] provided randomized evidence that the 100-mg dose seems to trend toward less dementia or cognitive impairment, but that it's not statistically significant, either for the broad or the narrow definition. Smaller dementia benefits could be present, but my take-home is that we don't use aspirin for primary prevention, and there's not compelling data that would make you think about it for dementia either.

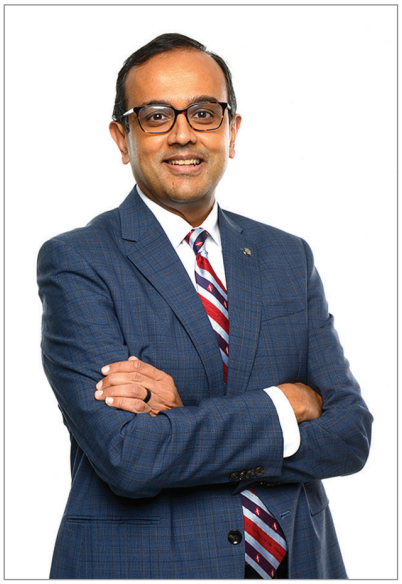
JAMA: Would the results potentially be any different in a cohort that did not have diabetes?

DR PATEL: Diabetes is a risk enhancer for vascular disease. Remember that vascular disease is an inflammatory atherothrombotic disease, and we are thinking about aspirin as an antiplatelet or antithrombotic. Usually if it's lower risk, then it's even less likely to show a benefit, so I'm not sure we would've seen different results.

JAMA: Let's talk about the EMPULSE (Efficacy And Safety of Empagliflozin in Hospitalized Heart Failure Patients) trial. This is an SGLT-2 [sodium glucose cotransporter 2] inhibitor that's already used to reduce the risk of cardiovascular death or heart failure hospitalization in patients who have chronic heart failure. This study asked about patients with acute heart failure who are in the hospital—does it help them?

DR PATEL: These drugs, these SGLT-2 inhibitors, have really taken the cardiovascular world by storm. They were originally studied in [people with] diabetes, and then it was identified that, lo and behold, they helped with heart failure. We've started to show that they broadly help people with heart failure, with or without a reduced ejection fraction or a weakened heart muscle.

Given that they've started to show that broadly and with multiple versions of these drugs in heart failure, the investigators here wanted to understand—does the drug, if you started it in the hospital after acute decompensated heart failure, reduce clinical events? They randomized more than 500 patients to usual care vs starting the drug in the hospital and looked over the next year to 2 years to see if it reduced cardiovascular disease death, hospitalization, and a variety of cardiovascular events. And in fact, the drug did, with a hazard ratio of 0.55. So it was a pretty significant reduction.



Manesh Patel, MD
Walter Johnson Jr/American Heart Association

JAMA: The next study we're going to talk about is the AVATAR (Aortic Valve Replacement Vs Watchful Waiting in Asymptomatic Severe Aortic Stenosis) trial. This study looked at patients with asymptomatic severe aortic stenosis (AS) and investigated whether aortic valve replacement or watchful waiting was better.

DR PATEL: We now sometimes identify people who have severe aortic stenosis who have yet to have symptoms. These investigators intended to find out, if you operate earlier on these patients, does it make a difference? In 7 European countries at 9 medical centers, they took 157 patients with severe AS who didn't have symptoms and put them on a treadmill. They showed that, even with exercising, they did not have significant symptoms. So a pretty important step. Then they randomized them to waiting vs going through aortic valve surgery. Those who went early to surgery had significantly less cardiovascular events, all-cause death, heart failure, acute MI, and stroke. There were not a ton of those events, but in the early surgery group there were 13 and in the conservative group there were 26. So over a 50% reduction in some of those events.

My sense is most people will now be a little bit more aggressive in patients that have aortic stenosis. Even if they're asymptomatic, they might get to surgery faster.

JAMA: New chest pain guidelines were discussed at the conference. What's new there?

DR PATEL: First, I commend the AHA and the American College of Cardiology in putting out chest pain guidelines. Chest pain is something every clinician at some point sees or thinks about, and yet these are the first official guidelines.

What might be the most important new thing is that the evolution of CT [computed tomographic] angiogram as a testing modality for patients in a variety of trials has moved it up in the guidelines to at least have it as a viable option early on as a first test.

JAMA: One of the interesting COVID-19–related studies at the meeting was about the disruption in blood pressure control during the pandemic in 24 US health systems.

DR PATEL: It was a really important blood pressure management study during COVID across PCORI, the Patient-Centered Outcomes Research Institute network in the United States, which are several health systems that, even before COVID, were sharing data on blood pressure management every 6 months.

Before COVID, in about 1.7 million people or so, [the percentage of patients meeting] the blood pressure goal was around 60%. When COVID hit, over the following 6 to 12 months, you can see that that blood pressure control went down about 10 full percentage points to the low 50s, high 40s. This is a substantial drop that we know unfortunately will lead to significant morbidity and mortality in the coming years as a sort of tsunami of cardiovascular disease. I think it was eye-opening.

JAMA: Did the study give any hints as to why blood pressure control really suffered during this time?

DR PATEL: It's likely because people avoided care for the reasons that we can all imagine because of COVID. During the data presentation, the months of May and June and July [2020], that quarter or so when there were stay-at-home orders and the start of understanding the pandemic, there wasn't as much data on blood pressure at those health systems. And then as they came back online with data, blood pressures were being measured much lower. And I'm sure it's both because of patients avoiding health care, but also because of the systems being so stressed. But we don't have actual data of that.

JAMA: In prior years, there have been big trials on omega-3 fatty acids for heart disease at scientific sessions. Now that the dust has settled a little bit on those trials, could you tell us where we've landed?

DR PATEL: We know through fairly large clinical trials that fish oil itself has not been shown to reduce cardiovascular events. But there is an agent called icosapent ethyl, which is a very high concentration of the omega-3s that are in fish oil—up to 2 g, twice daily. In REDUCE-IT (Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial), it did reduce cardiovascular events.

Patients ask me, "Should I be taking fish oil?" First, I think we want our patients to take lipid-lowering agents that we do first-line, like statin therapy or others. Then if they have residual risk with higher triglycerides, they might be candidates for icosapent ethyl. But over-the-counter nutritional fish oil at much lower doses I certainly am not recommending.

The icosapent ethyl trial was remarkably positive. There have been some conversations about the control group and other things. I still think there's a signal there and a clearly efficacious therapy. There are patients that benefit from that therapy, but I think of it as just like a statin therapy—a pill that has a high concentration of an agent in it. ■

Conflict of Interest Disclosures: Dr Patel has received research grants from AstraZeneca, Bayer, Janssen, Mytonomy, and Procyrion and serves on the advisory boards of Bayer, Janssen, and Novartis.

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