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DAILY NEWS

ScientificSessions.org *#AHA19*

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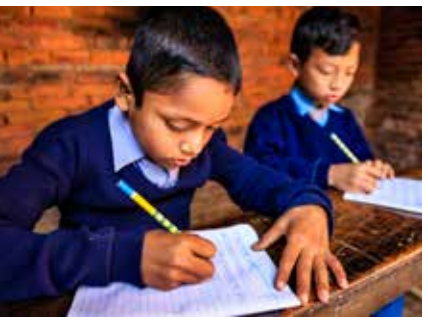

Echocardiographic screening of children may reduce burden of rheumatic heart disease

Echocardiographic screening of children for subclinical rheumatic heart disease and secondary antibiotic prevention in affected children may reduce the burden in endemic regions, according to an abstract presented Saturday.

In the study, researchers conducted a cluster-randomized comparison of echocardiographic

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ISCHEMIA

Early intervention vs. conservative therapy can improve angina symptoms, quality of life for patients with SIHDI and angina

Hochman

Researchers in "Results for the ISCHEMIA Trials: To Intervene or Not To Intervene" Late-Breaking Science session on Saturday found:

- Initial invasive therapy compared to optimal medical therapy in patients with stable ischemia heart disease and moderate-severe ischemia did not reduce the risk for cardiovascular events.
- Initial invasive therapy is more effective than optimal medical therapy in controlling angina and for QOL for patients with stable ischemic heart disease who have angina.
- For patients with advanced chronic kidney disease and stable ischemic heart disease, an initial invasive therapy does not improve risk for cardiovascular events versus optimal medical therapy.

ISCHEMIA clinical outcomes

An initial invasive strategy of routine catheterization and revascularization dis not demonstrate a reduction in risk for clinical events over 3.3 years of follow-up compared to an initial conservative strategy of optimal medical therapy for patients with stable ischemic heart disease (SIHD) and moderate to severe angina.

ISCHEMIA (International Study of Comparative Effectiveness with Medical and Invasive Approaches) was the most anticipated trial at Scientific Sessions, said moderator Elliot Antman, MD, professor of medicine at Harvard Medical School in Boston. Conflicting trial results left the profession in equipoise over the most appropriate approach to treating patients with SIHD and angina.

ISCHEMIA is the only trial to compare revascularization versus optimal medical therapy in patients with SHID and moderate to severe angina, said Co-Principal Investigator Judith S. Hochman, MD, Harold Snyder Family Professor and associate director of cardiology and co-director of NYU-HHC Clinical and Translational Science Institute at New York University NYU School of Medicine.

ISCHEMIA is also the largest trial to compare the two treatment strategies in SHID. Investigators randomized 5,179 patients with SHID and moderate to severe angina to optimal medical therapy alone or in combination with routine coronary revascularization by PCI or CABG if feasible. Patients were followed for a mean of 3.3 years.

Patients in earlier trials comparing invasive versus medical therapy had angiography prior to randomization, Hochman

See **ISCHEMIA**, page 13

Session to highlight importance of detecting peripheral artery disease early, improved protocols

Six experts will discuss the importance of detecting peripheral artery disease early and initiating prompt, targeted care.

The risk of developing coronary artery disease, heart attack or stroke is higher among an estimated 8.5 million Americans with PAD than in the general population. Those with PAD are also more likely to lose a limb.

Yet, many people with PAD don't know they have it. Some feel no pain, so they don't seek medical advice. Others write off their symptoms to age. And in some cases, health care professionals miss the signs.

"PAD is a common cardiovascular condition, yet it's often underdiagnosed and undertreated," said Geoffrey

See **PAD**, page 14

UPCOMING SESSION

A Sign of the Times for PAD: Stents, Drugs and Walk 'n' Roll
10:45 a.m.-Noon Sunday
Main Event II

Need to charge your device? Visit the Charging Lounge in the HEART Hub or one of the charging stations in Grand Hall, Level 2, and in the Broad Street Atrium, Level 1. *Sponsored by Amgen.*

Sunday's innovative sessions you don't want to miss

TIME	LOCATION	SUPPORTER	TITLE
10:15-11 a.m.	Learning Studio 2	Amgen, Inc.	Amgen: Cardiovascular Patient Cases
	Learning Studio 1	Janssen Invokana	CREDENCE Landmark Trial: Canagliflozin and Renal Endpoints in Diabetes With Established Nephropathy Clinical Evaluation Clinical Trial
Noon-12:45 p.m.	Heart Theater	Janssen Pharmaceuticals, Inc.	Evidence-Based Approach to Anticoagulation Therapy for NVAF
	Learning Studio 1	Amgen, Inc.	Getting to the Heart of the Matter: A Panel Discussion on New Data, Guidelines and What It Means for Managing Your Patients With MI
	Learning Studio 2	Novartis Pharmaceuticals Corp.	Worsening Symptoms and Hospitalization for Heart Failure: Increased Risk of Poor Outcomes and Opportunities To Enhance Care
	Game Central	Amgen, Inc.	A Life Worth Living: Health-Related Quality of Life in Heart Failure
1:15-2 p.m.	Heart Theater	Amgen, Inc.	Amgen: Cardiovascular Patient Cases
	Learning Studio 1	Novartis Pharmaceuticals Corp.	HFpEF Presentation by Novartis - TBC
	Learning Studio 2	Bristol-Myers Squibb and Pfizer	Undiagnosed AF: Continuing Developments
	Game Central	Amarin Pharma, Inc.	Expert Insights: Managing Cardiovascular Risk Based on the Landmark CV Outcomes Trial (REDUCE-IT™)
3:15-4 p.m.	Learning Studio 1	Portola	Reversal of Specific Direct Oral Anticoagulants in Patients Experiencing Life-Threatening Bleeds
	Learning Studio 2	Rise Above Heart Failure (3-4:30 p.m.)	Trends in Transitions of Care: Transforming the HF Patient Journey

ISCHEMIA

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said. Knowing a patient's coronary anatomy may have introduced bias in patient selection and treatment choices.

ISCHEMIA randomized patients without prior knowledge of coronary anatomy and used a predetermined threshold of baseline ischemia. After randomization, most patients (73%) had blinded coronary computed tomography angiography (CCTA) to assess their coronary anatomy.

The primary ISCHEMIA endpoint is a composite of cardiovascular death, myocardial infarction, hospitalization for unstable angina, hospitalization for heart failure or resuscitated cardiac arrest. Major secondary endpoints include the composite of CV death and MI; other secondary endpoints included all-cause mortality, net clinical benefit (primary and secondary endpoints combined with stroke), angina-related symptoms and disease-specific quality of life.

Patients in ISCHEMIA had a median age of 64; 22.6% were women, 41% had diabetes and 89.7% had a history of angina. The trial includes 33.7% nonwhite and 15.5% Hispanic patients. Patients were recruited following either stress imaging (75.5%) or non-imaging exercise tolerance testing (24.5%) across 341 sites in 38 countries.

Of patients in the stress imaging cohort, 44.8% had severe ischemia, 41% had moderate ischemia and 8.1% had mild ischemia. Six percent had no ischemia or could not be interpreted. Of patients in the exercising tolerance cohort, 83% had severe ischemia, 8% had moderate ischemia, 2.7% had mild ischemia and 6.3% had no or uninterpretable ischemia.

In the total population, 54% had severe ischemia, 33% moderate, 12% mild and 1% could not be interpreted. Follow-up data were available on more than 99% of patients in both arms.

There was no significant difference in the primary outcome of death, MI, hospitalization for uncontrolled angina, heart failure or resuscitated cardiac arrest: 15.% in the optimal medical therapy group and 13.8% in the invasive group (HR=0.93, p=0.34) at five years. There was a 1.9% advantage to conservative therapy at six months and a 2.2% advantage to invasive therapy at four years.

Clinical results for the secondary outcomes were similar, with a 2% advantage for conservative treatment at six months, a 2% advantage to invasive treatment at four years and no significant difference at five years.

Investigators found no heterogeneity of treatment effect in prespecified subgroups. The only difference was a small advantage to invasive treatment for patients with severe angina that was not seen in patients with none or moderate angina.

"There was low all-cause mortality in both groups," Hochman said. "But overall, an initial invasive strategy as compared to an initial conservative strategy did not demonstrate a reduced risk for clinical events."

ISCHEMIA quality of life outcomes

While an invasive strategy did not improve clinical events in ISCHEMIA patients, it did improve angina symptoms and quality of life for patients with daily, weekly, monthly angina at baseline.

Most patients in ISCHEMIA, 2,322 in the invasive group and 2,295 in the conservative group, were assessed for health status (symptoms and function) and quality of life at baseline, 1.5 months, three months and every six months thereafter for three years using the Seattle Angina Questionnaire (SAQ). SAQ completion rates were excellent (roughly 90% at three years for both groups), said John A. Spertus, MD, MPH, Saint Luke's Mid American Heart Institute at the University of Missouri, Kansas City.

Overall, patients in the invasive group reported numerically higher SAQ scores for angina frequency and quality, but the difference was not significant.

For patients with daily or weekly angina, the invasive strategy provided clear benefits from three months to three years. Patients with symptoms had a 15% probability of no angina in the conservative group versus 45% in the invasive group.

"The goal of treatment in patients with symptoms is to be angina-free," Spertus said. They had significant and durable improvements in angina control and quality of life with an invasive strategy if they had daily or weekly angina symptoms at baseline. Shared decision-making should be used to align treatment with patients' goals and preferences."

ISCHEMIA-CKD clinical outcomes

Clinical outcomes in patients with advanced chronic kidney disease mirrored those of the main ISCHEMIA population. There were no significant differences in clinical events between the invasive and conservative populations.

ISCHEMIA-CKD is the first large SIHD trial to include patients with CKD, said Sripal Bangalore, MD, MHA, professor of medicine at the New York University School of Medicine. Earlier trials systematically excluded CKD patients.

A total of 777 patients who were excluded from ISCHEMIA because of advanced kidney disease were enrolled in ISCHEMIA-CKD. In addition to the ISCHEMIA criteria, patients had an estimated glomerular filtration rate less than 30 or be on dialysis for end-stage renal disease.

As expected, patients in the invasive group had an elevated rate of procedural MIs and patients in the conservative group had more spontaneous MIs. The biggest difference between the two populations was the rate of stroke.

Patients in the invasive group had significantly more strokes (HR=3.76, p=0.004), but the excess strokes were not associated with revascularization procedures.

"An invasive strategy did not demonstrate a reduced risk of clinical outcomes compared with an initial conservative strategy," Bangalore said.

ISCHEMIA-CKD quality of life outcomes

An invasive approach made no difference in angina or quality of life scores compared to conservative treatment. Patients in the invasive group with daily or weekly anginashowed a small improvement in angina at three months, Spertus said.

"We have strong confidence in an early benefit from an invasive strategy," he said. "But we have very low confidence in any benefit in the longer term. We cannot exclude the possibility of a small benefit in patients with severe angina." •