Understanding the importance of age in selecting a testing strategy for stable symptomatic patients with suspected coronary artery disease: A prespecified analysis from the PRECISE randomized trial.

Evangelia Vemmou1, MD, Michelle D. Kelsey2, MD, Sreekanth Vemulapalli2, MD, Daniel B. Mark2, MD, Campbell K. Rogers3, MD, Sarah Mullen3, MBT, Whitney Huey3, BA, Karen Chiswell4, Ph.D., Robert M. Clare4, PhD, Eric Yow4, MS, Jonathon A. Leipsic5, MD, Robert A. Byrne6, MBBCh, PhD, Nicholas Ng3, BS, Kit Pier7, MS, James E. Udelson8, MD, Pamela S. Douglas1,4, MD, Michael G. Nanna9, MD, MHS

1.Yale New Haven Hospital, New Haven, CT, USA; 2. Duke University Medical Center, Division of Cardiology, Durham, NC, US; 3. HeartFlow, Inc., Mountain View, CA; 4. Duke Clinical Research Institute, Durham, NC, USA; 5. Division of Cardiology, Vancouver General Hospital, University of British Columbia, Vancouver, BC, Canada; 6. Mater Private Network, Dublin, Ireland; 7. PharPoint Research, Inc; Durham, NC;
8. Tufts University, Division of Cardiology, Boston, USA; 9. Section of Cardiovascular Medicine, Yale School of Medicine, New Haven, CT, USA

Yale Internal Medicine Residency Program, New Haven, Connecticut

♦ Background

Current chest pain guidelines state that cCTA may be preferred in people <65 years old who present with stable chest pain and are not on optimal preventive therapies, while stress testing may be advantageous in those ≥65 years old, who have a higher likelihood of ischemia and obstructive coronary artery disease (CAD). In PRECISE trial, a precision strategy (PS) with risk stratification and coronary CTA with FFRCT (CTA±FFRCT) was superior to usual testing (UT) for the primary endpoint of death, MI, or catheterization without obstructive coronary artery disease (CAD) at 1 year. We explored whether these results varied by age (< or ≥ 65 years old).

♦ Objective

To determine if there are age-related differences for evaluating adults with suspected CAD using a precision strategy vs. functional testing and evaluate the prognostic discrimination of CTA± selective FFRCT vs. functional testing for the diagnosis of obstructive CAD on cardiac catheterization in intermediate risk older (≥ 65) vs. younger (<65) adults.

♦ Questions

Are there any age-related differences for evaluating adults with suspected CAD using a precision strategy vs functional testing?

♦ Hypothesis

A precision evaluation strategy would result in lower number of catheterizations without obstructive CAD.

♦ Methods

In PRECISE trial, patients were randomized to PS or UT. Participants in the PS group with a PROMISE Minimal Risk Score (PMRS) threshold value ≥ 0.46 were assigned to an initial strategy of deferred testing (the higher the PMRS score, the lower the risk) and all others received cCTA ± selective FFRCT. We assessed the impact of age on 1) the primary endpoint for the entire cohort, and 2) on diagnostic performance for obstructive CAD in an intermediate risk subset (Figure 2) excluding the lowest and highest risk deciles according to PMRS.
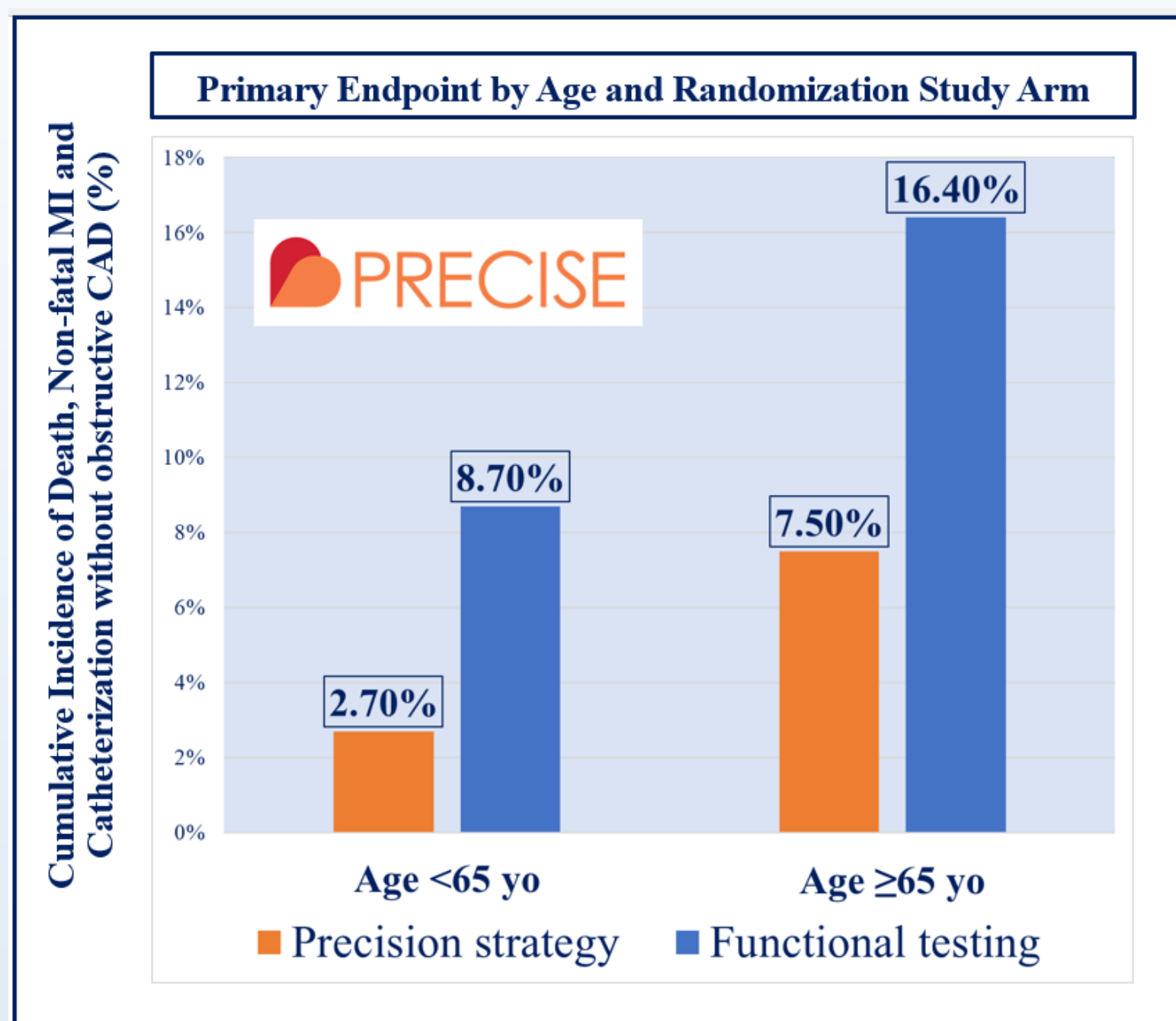
Primary Endpoint by Age and Randomization Study arm
The figure demonstrates the 12-month incidence of death, non-fatal myocardial infarction and invasive catheterization without obstructive coronary artery disease (CAD) in all participants of the PRECISE trial by age and randomization study arm.

♦ Results

Both younger (N=1430) and older patients (N=673) had lower primary endpoint rates with PS vs. UT(<65: 2.7% vs. 8.7%, HR 0.30, 95% CI 0.18-0.50; ≥65 7.5% vs. 16.4%, HR 0.43, 95% CI 0.27-0.69; p interaction=0.32). In the intermediate risk subset (n=1140) among patients undergoing a cardiac cath (n=111), a finding of obstructive CAD was associated with a previous positive CTA±FFRCT in most patients in both age groups (53.0% in <65, 72.5% in ≥65), but was infrequent among those with a previous positive stress test (26.1% in <65, 9.1% in ≥65). The adjusted association between test positivity and obstructive CAD on catheterization favored CTA±FFRCT over stress testing in both age groups (<65, HR 2.76 (1.45, 5.25); ≥65, HR 4.89 (1.07, 22.36)).
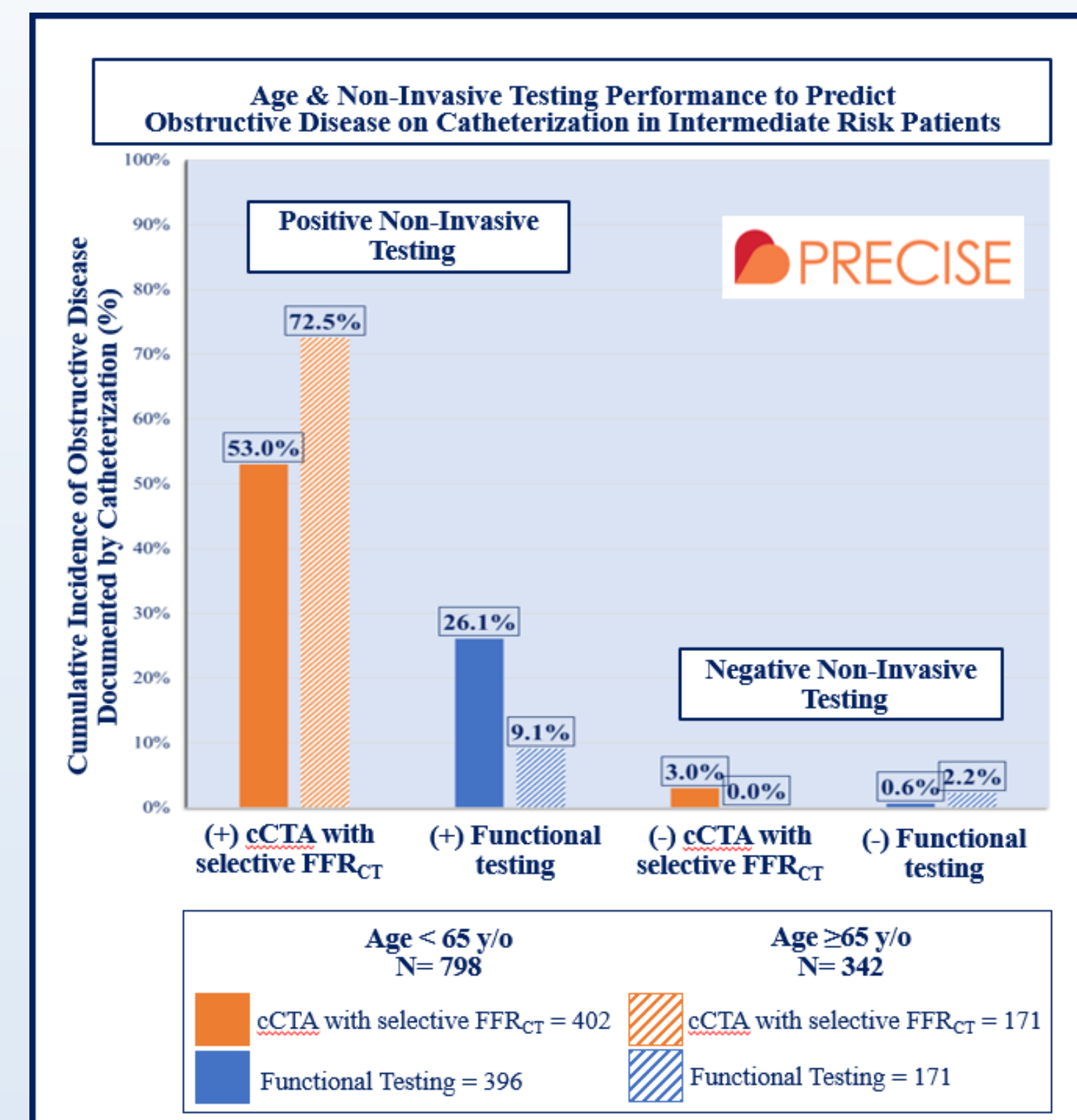
Age and Non-Invasive Testing Performance to Predict Obstructive The figure demonstrates the cumulative 12-month incidence of obstructive CAD documented by invasive catheterization among all intermediate risk patients with interpretable noninvasive test results by age and test type (CTA with selective FFRCT, vs. functional testing) in the PRECISE trial.

♦ Summary

In summary, the performance of a CTA±FFRCT based precision strategy was superior to usual testing for both younger and older patients. Moreover, among intermediate risk patients, CTA±FFRCT was a more efficient gatekeeper to the cath lab, identified by better identifying patients with obstructive CAD more frequently than a stress testing approach in both age groups, and especially in those ≥65.

♦ Limitations

First, like the original study, the relative discrimination of cCTA with FFRCT was not compared to individual stress testing modalities, so the relative prognostic performance of those unique modalities cannot be determined. Second, we were limited by the low event rates and also sample size of patients within the age sub-groups who underwent cardiac catheterization in PRECISE, though the association between test positivity and obstructive CAD on cardiac catheterization achieved statistical significance for the PS vs. UT in both age groups despite the limited sample.

♦ Strengths

-Randomized design
-the addition of selective FFRCT to cCTA increases the performance of an anatomic diagnostic strategy by introducing the advantages of physiology to regulate downstream invasive testing and improve clinical efficiency

♦ Conclusions

In PRECISE, the performance of CTA±FFRCT was superior to usual testing for both younger and older patients. Moreover, among intermediate risk patients, CTA±FFRCT identified patients with obstructive CAD more frequently than a stress testing approach in both age groups, and especially in those ≥65.