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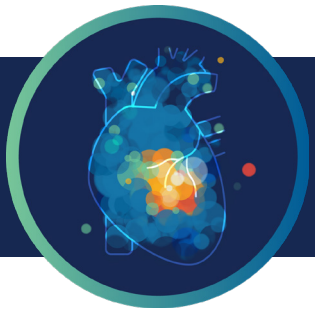
EXPERT INSIGHTS: Q&A WITH DR. MIRVAT ALASNAG



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Despite significant strides made in the early detection, prevention and pharmaceutical and/or interventional treatment of coronary heart disease, it remains the number one cause of mortality globally. Why do you think this is the case?

I believe we intervene late. These patients come to our attention once they've had their first or even second event. At this point we seek to intensify our preventive measures and to investigate underlying reversible causes. We really haven't availed ourselves of the advances in early detection and prevention adequately.

What were the key take home messages from the ORFAN Study?

The trial noted that among patients undergoing computed tomography coronary angiography (CTCA), the majority of events occur in those who do not have obstructive coronary artery disease (CAD). It also indicated that measuring coronary inflammation from CTCA (Fat Attenuation Index - FAI - Score) can predict fatal and non-fatal cardiac events, independently from clinical risk scores and routine CCTA interpretation. The AI-Risk model (FAI Score + plaque + risk factors) reclassifies approximately 30% to a higher and approximately 10% to a lower risk category. Furthermore, when presented to clinicians, a change of management occurs in half of the patients.

What are the important limitations of this study in your view?

The most important limitation is generalizability to ethnicities and geographies not included in the trial. These can obscure current risk stratification models particularly when confounded by optimization of risk modifying agents, age and recurrent ASCVD events. The other more obvious limitation would be the widespread availability of CCTA and the added cost of these tests.

A prospective real-world survey of 744 patients from the ORFAN study showed that application of the AI-Risk Classification model versus standard of care clinical management, reclassified approximately 30% of the cohort to a higher risk category. This then stimulated changes in clinical management of the patient. Given the evidence supporting colchicine in the secondary prevention of ASCVD, its low cost, and favorable safety profile (if gastrointestinal upset can be tolerated), is there an argument for its widespread long-term use irrespective of the degree of coronary inflammation?

Perhaps the resistance would be tolerance of colchicine rather than cost. An additional dilemma is polypharmacy in patients who have already had an event. ASCVD patients are usually on a large number of agents all which have proven to reduce cardiovascular mortality including lipid lowering therapy, antiplatelet drugs, anticoagulants such as rivaroxaban (COMPASS trial) in addition to the other medications for left ventricular dysfunction which many of our patients have (now 4 pillars).

Therapies targeting coronary inflammation to treat atherosclerotic cardiovascular disease (ASCVD) have gained notable traction in the last few years. And as further novel agents undergo clinical development, is there a sweet spot in the continuum of ASCVD pathophysiology that they may realize their most beneficial effect? Primary prevention in those with a strong risk factor profile, in the immediate aftermath of an acute coronary syndrome or secondary prevention of recurrent events in those with established ASCVD?

At this time, I suspect the uptake would be higher in two categories of patients: those who have recurrent events and those with a family history of premature coronary artery disease. Perhaps young patients with residual risk ought to be considered as an early intervention.

Artificial intelligence was used to estimate the Fat Attenuation Index in the ORFAN Study, as a measure of perivascular inflammation around the coronary arteries and it is also being used to assess the morphology and burden of coronary plaque, from a CTCA. Both are showing promise as AI-derived markers of the risk of future cardiovascular morbidity and mortality. Where do you think the next frontier is for artificial intelligence in the management and/or prevention of ASCVD?

We need to recognize that risk assessment should be a longitudinal endeavor and not a mere one time cross-sectional scoring system. Patients need to be re-stratified regularly as they develop new ASCVD risk factors or sustain new events. A tailored individualized longitudinal assessment of risk is key. Additionally, a population wide indicator of risk reduction in a given community will permit health authorities to address intervention priorities. At this time, >85% of health expenditure in developed countries is assigned to secondary prevention leaving only 15% for primary prevention. AI tools may tip the balance whereby primary prevention measures are allocated in larger amounts (It is also noteworthy that most primary prevention interventions are cheaper and often service a larger proportion of the population).