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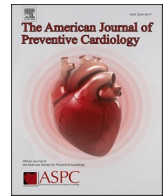
Cardiac CT, a friend and guide in cardiovascular prevention: Fellow's Voice

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In the widely acclaimed documentary "Widowmaker", Larry King, television and talk show host, famously spoke about how he felt completely fine, before being diagnosed with heart disease requiring bypass surgery. He noted how his experience was rather different from the 'Hollywood heart attacks' – a commonly depicted scenario of an elderly man who clutches his chest and is acutely short of breath. Unfortunately, such patient stories like Mr. King's are not unheard of. Despite remarkable strides in diagnostics and treatment in cardiology, identifying precise markers of cardiovascular (CV) risk assessment and their translation to prevention, remain one of the most pressing challenges today. Evidence to date indicates that traditional risk factors alone fail to accurately stratify asymptomatic individuals who are at high risk for atherosclerotic cardiovascular disease (ASCVD) events [1]. Advances in non-invasive imaging particularly cardiac computed tomography (CT) have provided opportunities to detect subclinical atherosclerosis, a long latent phase of clinically unapparent coronary lesions, wherein patients are usually asymptomatic [2,3].

Coronary artery calcium (CAC), a highly specific surrogate for subclinical atherosclerosis, is detected by non-contrast cardiac CT as calcified plaque in coronary arteries. Multiple studies have demonstrated that presence, extent and severity of CAC provide significant prognostic information, beyond traditional risk factors [4]. Extensive research from validated cohorts have shown that the CAC score is indeed one of the best predictors of absolute risk of 10-year ASCVD events in intermediate risk asymptomatic individuals, but also can refine risk prediction across all risk categories in primary prevention. Importantly, a CAC score of zero has been associated with an extremely low risk of future adverse CV events, including stroke and mortality, over 10–15 years [5]. It should be noted that a CAC score of 0 is indeed associated with a low risk of ASCVD events in next 5–10 years, but not "no risk" and should not supersede clinical judgement. Nevertheless, CAC's superior ability to refine risk prediction, not only to upgrade risk when prevalent, but also its potent ability to "de-risk" individuals to a lower risk category when the score is zero, has led to its adoption in more recent American College of Cardiology (ACC)/American Heart Association (AHA)

guidelines on the management of blood cholesterol and primary prevention of CV disease in cases of risk uncertainty. These guidelines state that CAC=0 could be used to downgrade risk and defer statin therapy in borderline/intermediate risk individuals, except in smokers, those with diabetes mellitus, and those with a strong family history of premature ASCVD (class IIb) [6,7]. The guidelines also recommend statins for any patient ≥55 years of age with CAC score of 1–99 (class IIa). Furthermore, a CAC score ≥100 Agatston units or ≥75th percentile for age/sex favors statin initiation. The promise of CAC in CV prevention continues to evolve, as ongoing studies hope to address the role of CAC in clinical trial enrichment and whether its use as a risk-decision tool improves subsequent clinical outcomes and cost effective preventive care, to increase its adoption and widespread clinical use [8].

Coronary computed tomography angiography (CCTA) is also emerging as an extremely useful non-invasive test in diagnosis of stable coronary artery disease (CAD), and as a tool to guide CV interventions *and* prevention [9]. Insights from major clinical trials such as SCOT-HEART (Scottish Computed Tomography of the HEART) and PROMISE (Prospective Multicenter Imaging Study for Evaluation of Chest Pain) have paved the way for role of CCTA as the first step in evaluation of low or intermediate risk patients with stable CAD. A 'CCTA first' strategy for evaluation of stable chest pain in low to intermediate risk patients, is now endorsed by multiple societies [10]. The principle advantage of CCTA in evaluation of these patients includes its ability to detect and characterize non-obstructive coronary atherosclerosis in various stages, that have been correlated with adverse CV outcomes. Consistent with the natural history of coronary plaque progression and instability/rupture, the PROMISE trial showed that nearly 77% of myocardial infarctions and CV deaths were observed in patients with non-obstructive CAD by CCTA [11]. In addition, the superior prognostic value of anatomic assessment of coronary atherosclerosis has been shown in COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) and ISCHEMIA (International Study of Comparative Health Effectiveness with Medical and Invasive Approaches), where increasing severity of atherosclerotic disease defined

by CCTA correlated with risk of adverse events [12,13]. In this context, CCTA provides an opportunity for not only the exclusion of obstructive disease but also for early identification of non-obstructive disease and initiation of preventive strategies including aspirin, statins and risk factor modification. The presumed mechanism of CV benefit in SCOT HEART trial has been attributed to the early initiation of preventive medications in patients with non-obstructive CAD on CCTA, unlike those who underwent stress testing [14]. Emerging evidence of CCTA and its applications based on CT derived fractional flow reserve, plaque characterization and artificial intelligence will continue to support its role as an important tool in CV prevention.

There is an urgent unmet need for a paradigm shift in our approach to CV prevention – cardiac CT allows for a novel approach of personalized risk assessment and targeted prevention, by characterization of subclinical atherosclerosis as a phenotypic surrogate of the 'vulnerable patient'. As Drs. Vijay Nambi and Deepak Bhatt eloquently asked an important question in their editorial titled, "Primary Prevention of Atherosclerosis: Time to Take a Selfie?" [15]; I would say – Yes! The time for prevention is now and let's consider that selfie with Cardiac CT!

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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