Commentary

The impact of age & ethnicity in coronary artery disease risk assessment using Framingham Risk Scores & metabolic syndrome

Metabolic syndrome (MS) is a constellation of coronary artery disease (CAD) risk factors including abdominal obesity, non-traditional dyslipidaemia [i.e. low high density lipoprotein cholesterol (HDL-C), high triglycerides (TG) levels and the presence of small, dense low density lipoprotein cholesterol (LDL-C) particles], impaired fasting glucose and elevated blood pressure. These abnormalities tend to cluster in a frequency greater than chance expectation and it was hypothesized that the underlying pathophysiological disorder is insulin resistance¹. Epidemiological data derived from large, community-based observational studies suggest that MS is associated with incident diabetes mellitus² and increased cardiovascular (CV) morbidity³ and mortality⁴. However, these findings were questioned by others claiming that MS has no independent predictive ability for future CV events^{5,6} or that MS carries no additional prognostic information than that conferred by the sum of its parts⁷.

On the other hand, Framingham Risk Score (FRS) is a widely accepted risk model estimating one's 10year cardiovascular risk and stratifying individuals accordingly as low (<10%), intermediate (10-20%) and high risk (>20%)⁸. FRS takes into account age, smoking status, lipids, diabetes status and hypertension. Prospectively collected data support that FRS is superior to MS in future CV events prediction⁹ while others report a significant correlation between MS and prevalent CAD in subjects considered as low risk according to FRS¹⁰.

In the present cross-sectional study by Khanna *et al*¹¹, both MS status and FRS were assessed in a consecutive sample of 200 patients undergoing coronary angiography. Among study participants, 88 per cent had significant coronary artery lesions defined as luminal narrowing of >50 per cent in at least one of the three major epicardial coronary arteries. MS was

significantly associated with CAD prevalence since only 6 per cent of MS patients had a normal coronary angiogram compared with 28 per cent of their non-MS counterparts (P<0.05). MS presence was also correlated with CAD severity with a reported prevalence of double or triple vessel disease of 61 per cent compared to 41 per cent among non-MS individuals (P<0.05). Despite this high overall CAD prevalence, as many as 35 and 41 per cent of patients respectively were classified as lowand intermediate-risk according to FRS. Mean FRS among MS patients, was significantly higher compared to those without MS (P<0.001) while MS prevalence increased progressively across FRS categories (from 61 over 87% to 92%).

The present work provides two useful clinical implications. First, the authors underline the significant age dependence of FRS which limits its predictive ability when it is applied in younger individuals. Splitting the patients into four age groups further supported this argument; MS prevalence remained constantly high (>70%) in all age groups while less than 15 per cent of patients younger than 65 yr were considered as having a high 10-year CV risk according to FRS¹¹.

The great importance of applying the more relevant MS definition for a certain population is another point highlighted in this study. Various guidelines have been proposed over time (*e.g.* WHO, NCEP-ATP, IDF) and different cut-off points have been set for certain ethnic groups. Particularly in Asians, a lower threshold for waist circumference is applied reflecting the overall lower mean BMI in this population. Moreover, a significant proportion of Asian people are described as metabolically obese - having high triglycerides and low HDL-C levels - while being within the normal range of waist circumference and waist-to-hip ratio¹².

Different MS definitions result in quite variable estimates for MS prevalence. In the present study¹¹, MS prevalence was 77 per cent according to the modified South Asian guidelines^{12,13} and came down to 61 per cent when IDF definition¹⁴ was applied. This observation suggests that considering the increased waist circumference as an essential criterion (IDF definition) would underestimate the true prevalence of MS in study's population. According to the authors, 12 per cent of participants with a normal BMI (*i.e.* <23 kg/m²) were still classified as having MS. Probably this subgroup of patients represents the normal weight but metabolically obese Indians.

The authors conclude that in a population where CAD develops earlier than it is reported in Western countries, FRS may underestimate true CV risk among younger individuals. On the contrary, MS prevalence remains constantly high across all age groups. Moreover, MS provides life-time prognostic information for incident CAD while FRS is valid only for a 10-year period which is a relatively short period when applied in young individuals. Based on the present study's findings, physicians should not rely solely to FRS to assess one's individual risk for future CV events rather evaluating additionally his/her MS status. Keeping in the same line, Khanna et al¹¹ underscore the need for increased awareness among health practitioners in diagnosing MS since a non-negligible proportion of patients may still have MS despite being of normal weight. In modern times where MS and associated metabolic abnormalities are constantly rising, early MS identification and adaptation of a healthier lifestyle seem to be the key goal for CV primary prevention.

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