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Paradoxically simple: A new nutritional index for predicting coronary risk★

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“If we could give every individual the right amount of nourishment and exercise, not too little and not too much, we would have the safest way to health”

– Hippocrates

Over two millennia ago, Hippocrates understood the balance of nutrition and health outcomes. Yet today, coronary artery disease (CAD) remains a leading cause of mortality world-wide, spurred by an ever-increasing obesity epidemic and its associated co-morbidities. Although hypercholesterolemia and high body mass index (BMI) are conventional cardiovascular risk factors, an “obesity paradox” has been observed in CAD patients, including those undergoing percutaneous coronary intervention (PCI), wherein a J-shaped relationship between BMI and mortality exists: patients with the lowest BMI, characterized by low lean body mass, suffer the highest cardiovascular event rates [1,2]. While risk stratification of patients following PCI based on nutritional status may provide useful prognostic information, no single nutritional index to date has been integrated into routine clinical use in patients with CAD.

Previously, the Geriatric Nutritional Risk Index ($GNRI = 14.89 \times \text{serum albumin (g/dL)} + 41.7 \times \text{body weight / ideal body weight}$), CONTrolling NUTritional status ($CONUT = \text{serum albumin (g/dL)} + \text{total lymphocyte count (per mL)} + \text{total cholesterol (mg/dL)}$), and the Prognostic Nutritional Index ($PNI = 10 \times \text{serum albumin (g/dL)} + 0.005 \times \text{total lymphocyte count (per mL)}$) have been evaluated as predictors of CAD patient outcomes. In an all-comers study of patients undergoing PCI, a low GNRI, indicating worse nutritional status, was associated with a higher incidence of all-cause (HR 1.30–1.84; $p < 0.0001$) and cardiac mortality (HR 1.08–1.90; $p = 0.01$) [3]. In another study of stable angina patients undergoing PCI, malnourished patients characterized by a higher CONUT score had more major adverse cardiac events (HR 1.30–2.07; $p < 0.0001$) [4]. Similar associations between low PNI, a marker of poor nutrition, and increased mortality have been observed in stable CAD patients following PCI or coronary artery bypass grafting [5,6]. Despite these observed associations with hard outcomes, nutritional indices have not gained traction in clinical

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practice in part because they employ parameters, such as serum albumin and total lymphocytes, which are not routinely collected in CAD patients.

In this issue of the *International Journal of Cardiology*, Doi and colleagues present “A novel and simply calculated nutritional index serves as a useful prognostic indicator in patients with coronary artery disease”, unveiling a newly-defined nutritional index the investigators have coined TCBI. TCBI incorporates triglycerides (TG), total cholesterol (TC), and body weight (BW), and is easily calculated according to the following formula: $TCBI = (TG \times TC \times BW) / 1000$. In this retrospective analysis of a cohort of ~3500 patients that underwent PCI at a single Japanese center, the capacity of TCBI to predict mortality was investigated in detail. In the unadjusted analysis, over a median of 6.3-year follow-up period, the primary endpoints of cardiovascular (HR 1.88–3.25; $p < 0.001$), cancer (HR 1.09–2.15; $p = 0.014$) and all-cause mortality (HR 1.80–2.59; $p < 0.001$) were higher in the lowest TCBI quartile, corresponding to patients with the poorest nutritional status. Additionally, the authors meticulously performed multivariate analyses that adjusted for age, gender, diabetes, chronic kidney disease, acute coronary syndrome (ACS) presentation, multi-vessel disease, and the use of beta blockers and statins. Consistent with the unadjusted findings, the multivariate results demonstrated that the lowest quartile TCBI was associated with greater cardiovascular (HR 1.29–2.37; $p < 0.001$) and all-cause mortality (HR 1.29–1.94; $p < 0.001$). In a propensity score analysis matched based on age, gender, ACS presentation, and statin use, patients in the lowest TCBI quartile also showed higher cardiovascular and all-cause mortality compared to patients in the other TCBI quartiles. Finally, the authors found that $TG \times TC \times BW$ performed better than any metric alone, and that including height-normalization by using BMI did not improve TCBI discrimination over simply using BW in this population.

Interestingly, despite their higher cardiovascular mortality, patients with a lower TCBI in this study had a lower prevalence of hypertension, dyslipidemia, and also lower HbA1C levels. These findings suggest that in this group of patients with low TCBI and fewer traditional cardiovascular risk factors, malnutrition contributes substantially to poor outcomes once significant CAD develops. Stratification of patients according to TCBI may therefore offer opportunities to identify a unique group of high-risk patients with potentially different therapeutic targets. On the contrary, high TCBI was associated with a protective effect against mortality by multivariate analysis (HR 0.77–0.96; $p < 0.001$), potentially representing the TCBI equivalent of the obesity paradox.

In summary, Doi et al. have crafted a promising new nutritional index tested in a large observational study with mortality endpoints. As nutritional status is an important marker of overall fitness, the results of this study hold the potential to offer TCBI as a novel prognostic indicator for CAD patients. The routine cardiology clinical variables utilized in TCBI allows it to be readily calculated in clinical cardiology practice, in contrast to previously studied nutritional indices. Supporting the generalizability of calculating TCBI in cardiovascular populations, values for TG, TC and BW were available in >99.7% of consecutive patients undergoing PCI at the study institution. In comparison, laboratory data on serum albumin (required for GNRI, CONUT, and PNI) was present in only ~80% of subjects. Given the current findings are from a single Japanese center, TCBI should be validated in larger, multi-

institution cohorts and other cardiovascular populations, such as those primarily following a Western diet where the obesity epidemic runs rampant. Of particular interest may also be chronic heart failure patients, where identification of nutritional decline manifest by cardiac cachexia is a hallmark of clinically advanced disease with a poor prognosis [7]. Further efforts should also focus on how longitudinal changes in TCBI over time impact cardiovascular outcomes, and whether TCBI-defined risk is modifiable, through specific nutritional, exercise, and pharmacotherapeutic interventions. In an era focused on promoting lifestyle changes to improve long-term cardiovascular health, if validated further, incorporating prognostic data from a simple nutritional index such as TCBI into the current clinical framework would likely be easily achieved, and may provide additional persuasive objective data that sways patients to chart a heart-healthier course.

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