

## Editorial



# “Obesity and Lean Paradox” in Peripheral Artery Disease

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Obesity is a strong risk factor for the development of cardiovascular disease (CVD).<sup>1</sup> However, at the same time, patients with many types of CVD may have a better prognosis if classified as overweight or obese.<sup>2</sup> This reversal has been so-called as “obesity paradox”, and well documented in numerous studies.<sup>3</sup> Although previous studies have reported inverse relationship between obesity and outcomes among patient with peripheral artery disease (PAD),<sup>4,5</sup> there remains debates whether the obesity paradox still works for the PAD patients who experienced endovascular therapy (EVT).

In this issue of *Korean Circulation Journal*, Lim et al.<sup>6</sup> present prognostic implications of body mass index (BMI) at 3-year follow-up from a nationwide, large-scaled multi-center registry, the Korean Vascular Intervention Society Endovascular therapy in Lower Limb Artery diseases. Among 2,914 PAD patients who were treated EVT, 7% of patients (204 patients) were underweight (BMI <18.5 kg/m<sup>2</sup>), 26.3% of patients (766 patients) were overweight (BMI 25–30 kg/m<sup>2</sup>), and only 4.3% of patients (126 patients) were obese (BMI ≥30 kg/m<sup>2</sup>). Unlike with previous studies, which adopted the definition of obesity for Asian subpopulations, the investigators defined obesity using World Health Organization criteria.<sup>7</sup> Nevertheless, patients with overweight showed significantly lower risk (adjusted hazard ratio [HR], 0.706; 95% confidence interval [CI], 0.537–0.928, p=0.013) of major adverse cardiovascular events (MACE) at 3 years, whereas patients with underweight showed significantly higher risk of 3-year MACE (adjusted HR, 1.539; 95% CI, 1.079–2.193; p=0.017) compared with those with normal weight. Additionally, underweight was independently associated with an increased risk of major adverse limb events (MALE) at 3 years (adjusted HR, 1.510; 95% CI, 1.056–2.160; p=0.024).

The authors are congratulated for their accomplishment of this study and for establishing the clinical relevance of BMI in PAD patients undergoing EVT. However, the results should be interpreted carefully, taking into account several limitations of the study. First, although BMI is generally used for defining obesity, there are limitations in its prediction power for assessing body fat for each individual. Notably, there is variation according to race/ethnicity, and country-specific cut points have developed.<sup>3</sup> Since this study has adopted for World Health Organization criteria, the prevalence of obesity in study population was relatively low (4.3%) compared with the previous study.<sup>4</sup> Second, BMI is not fully reflected the body components, including visceral fat, subcutaneous fat, or skeletal muscle mass. As a result, the presence of metabolic syndrome and CVD in a normal-weight individual who has excess body fat can be misdiagnosed

**Data Sharing Statement**

The data generated in this study is available from the corresponding author upon reasonable request.

**Author Contributions**

Conceptualization: Lee SH, Kim JH; Data curation: Kim JH; Investigation: Kim JH; Methodology: Kim JH; Project administration: Kim JH; Supervision: Kim JH; Writing - original draft: Lee SH; Writing - review & editing: Lee SH, Kim JH.

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or underestimation as not obesity classified by only BMI.<sup>3,8)</sup> Although a convenient index such as waist (or abdominal) circumference is available for evaluating central obesity, this parameter can not be addressed in this study. Third, the authors suggest malnutrition or sarcopenia as the major driven factor for increasing the MACE and MALE, but they can not address any parameters for assessing these effects. Even considering these limitations, it is certain that BMI has strong correlations between total body fat, visceral fat, or muscle mass and the only index widely adopted for evaluating obesity in contemporary practice.

The current study recognizes and provides clinical evidence of BMI as a continuum. Cubic spline regression analysis clearly demonstrates a negative non-linear association between BMI and the risk of MACE or MALE. Regarding this relation, the investigators finally confirm that underweight is a strong independent predictor of poor prognosis at 3 years. Rather than an obesity paradox, it is possible that this finding may represent a “lean paradox,” in which normal-weight or underweight patients show a higher risk of adverse events after CVD, as a result of a progressive catabolic state and lean mass loss.<sup>2)</sup> Unlike the debates of cut points for overweight/obesity, the cut point for underweight is firmly defined as less than 18.5 kg/m<sup>2</sup>. Therefore, the risk from underweight, which documented in this study, can be considered without racial and regional differences.

In summary, although there remains debate on the predictability of BMI for obesity according to race and ethnic differences, BMI has clinical impact on PAD patients undergoing EVT. As a continuous variable, BMI has a negative non-linear association with the risk of 3-year MACE or MALE after EVT. Both the “obesity paradox” and “lean paradox” should be considered for predicting outcomes among patients with PAD and undergoing EVT.

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