







# From the Obesity Tsunami to the Diabetes Avalanche: Primordial Prevention of the Diabesity-Related Cardiovascular Epidemic by Diabeto-Cardiologists

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## Keywords

diabetes, prediabetes, obesity, diabesity, diabeto-cardiologist

We thank Demirtas et al<sup>1</sup> for their interest in our paper entitled “Association of Prediabetes With Higher Coronary Atherosclerotic Burden Among Patients With First Diagnosed Acute Coronary Syndrome”<sup>2</sup> about the association of prediabetes with higher coronary atherosclerotic burden among patients with first diagnosed acute coronary syndrome (ACS). Demirtas et al<sup>1</sup> expressed some concerns about whether this coronary atherosclerotic burden in patients with ACS is related to “diabesity” or was “obesity” dependent.

The “diabesity” epidemic is likely to be the biggest epidemic in human history.<sup>3</sup> Due to the strong association of obesity with diabetes mellitus (DM),<sup>4</sup> the term “diabesity” has become popular to describe the specific form of DM (“obesity-dependent diabetes”) that develops late in life and is associated with obesity.<sup>5</sup> In many instances, obesity is the proximal trigger that culminates ultimately in DM and coronary artery disease (CAD).<sup>6</sup> Whereas the prevalence of obesity in the United States was 39% in adults, the prevalence of DM was reported as 14% in 2017.<sup>7</sup> Therefore, it is uncertain why not all people who are obese develop type 2 DM and why not all people with type 2 DM are obese.<sup>8</sup> There are many types of DM, but type 2 DM accounts for >90% of cases globally and diabesity usually relates to type 2 DM, which is also highly heterogeneous.<sup>9</sup> Anyone who is overweight and/or obese has some degree of insulin resistance, but DM only develops in those who lack sufficient insulin secretion to match their insulin resistance.<sup>10</sup> Since evidence exists in favor of the thesis that by the time of diagnosis of type 2 diabetes 80% of  $\beta$ -cell function is already lost,<sup>11</sup> intervening with therapies designed to interrupt the pathophysiological mechanisms that lead to type 2 DM is essential. Despite all, obesity represents approximately 44% of the attributable risk of DM, and without addressing it specifically at a population level, nearly one quarter of world’s population will be obese by 2045,<sup>12</sup> increasing the burden of DM and CAD.<sup>13</sup> There is mostly a one-directional

relation from obesity to DM, but not vice versa,<sup>14</sup> even if the patients with DM lose less weight than similarly obese patients without DM.<sup>15</sup>

Furthermore, systematic reviews of high-quality and consistent evidence show that the use of body mass index (BMI) to define obesity is highly specific, but has low to moderate sensitivity.<sup>16,17</sup> Although it is a simple, convenient, and noninvasive surrogate measure of body fat, it is a measure of excess weight per height rather than a direct measure of fat mass.<sup>18</sup> Therefore, there is no demonstration of an “obesity paradox” based on a direct measurement of body fat contrast to use of BMI as an index of obesity.<sup>18,19</sup> The waist to hip circumference ratio (normally <0.95 for men and <0.85 for women) is generally a better prognostic indicator for disease than the BMI,<sup>20</sup> especially when the BMI is <35.<sup>21</sup> A genetic predisposition to abdominal adiposity evaluated by higher waist to hip ratio adjusted for BMI was associated with increased risk of type 2 DM and CAD.<sup>22,23</sup> Elagizi et al discussed the utility and limitations of BMI for cardiometabolic risk stratification,<sup>24</sup> and Gregory et al reported no association of BMI with 1-year all-cause or cardiac-specific mortality after adjustment for potential confounding variables such as DM.<sup>25</sup> Although Asians with DM and ACS are less likely to be obese than their white counterparts, their risk of death or recurrent ischemic events was not lower.<sup>26</sup> Although obesity is often considered a relatively “minor” CAD risk factor, weight loss is a broadly effective

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intervention by influencing a number of “major” risk factors, especially DM and hypertension.<sup>27</sup>

All of this needs to be taken into consideration when interpreting diabetes trials.<sup>18</sup> A study outcome can be statistically significant, but not clinically significant and vice versa.<sup>28</sup> Diabetes and DM are often used interchangeably and there is a need to decide which factors are confounders before applying any statistical correction method. One of the fundamental assumptions underlying analysis of covariance (ANCOVA) is that of no interaction between factor and covariate. Due to mostly one-directional relation from obesity to DM but not vice versa,<sup>14</sup> the ANCOVA analysis was not considered suitable for adjustment for obesity due to the diabetes interaction. However, in the light of the author’s request, we analyzed, by ANCOVA tests, the influence of the BMI on Gensini and SYNTAX scores and whether HbA<sub>1c</sub>-based classification effects were retained regardless of “body weight” influence. The results remained significant after adjusting for BMI for both SYNTAX ( $F = 7.72, P < .01$ ) and Gensini scores ( $F = 6.95, P < .01$ ). Since we included patients with previous DM on antidiabetic or insulin therapy into the DM group, it would not be appropriate to compare HbA<sub>1c</sub> levels between the DM and prediabetic groups.

Type 2 DM will remain one of the greatest challenges to human health for many years to come, and the primordial prevention of the obesity tsunami would be a major strategy for reducing the DM avalanche.<sup>29</sup> Therefore, it is urgent to take steps including screening, prevention, and early management in an attempt to control this evolving epidemic of diabetes.<sup>30-33</sup> The most recent guidelines by the European Society of Cardiology in collaboration with European Association for the Study of DM recommend that all patients with ACS should be screened for DM.<sup>34</sup> Looking to the future, it has been suggested that the “thrombocardiologist” of the 20th century is being replaced by the “diabeto-cardiologist” of the 21st century.<sup>35</sup> Because the cardiologist often may be the first clinician to diagnose patients with ACS with DM or prediabetes,<sup>36</sup> it is incumbent upon them to understand the disease process and the interventions necessary to improve outcome.<sup>37</sup>

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