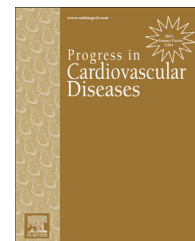


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## Potential Benefits of Weight Loss in Coronary Heart Disease

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### ABSTRACT

The prevalence of overweight, obesity and insulin resistance in patients with coronary heart disease (CHD) exceeds that of the general population. Obesity is associated with a constellation of coronary risk factors that predispose to the development and progression of CHD. Intentional weight loss, accomplished through behavioral weight loss and exercise, improves insulin sensitivity and associated cardio-metabolic risk factors such as lipid measures, blood pressure, measures of inflammation and vascular function both in healthy individuals and patients with CHD. Additionally, physical fitness, physical function and quality of life all improve. There is evidence that intentional weight loss prevents the onset of CHD in high risk overweight individuals. While weight loss associated improvements in insulin resistance, fitness and related risk factors strongly supports favorable prognostic effects in individuals with established CHD, further study is needed to determine if long-term clinical outcomes are improved.

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Obesity and overweight are highly prevalent in patients with coronary heart disease (CHD). Whereas the prevalence of overweight and obesity in the general U.S. population are at 66% and 36% respectively,<sup>1</sup> their prevalence, as with other coronary risk factors, is amplified in the CHD population. Overweight and obesity rates in patients with CHD entering cardiac rehabilitation (CR) are more than 80% and 44%, respectively.<sup>2</sup> From 1996 to 2006 the mean body mass index (BMI) of individuals with CHD entering CR has increased from 28.5 to 30.1 kg/m<sup>2</sup>, with a 33% increase in the prevalence of obesity (BMI > 30 kg/m<sup>2</sup>).<sup>2</sup> While obesity is an independent risk factor for the development of CHD,<sup>3</sup> it also predicts an elevated risk through its association with a cluster of risk factors termed the metabolic or insulin resistance syndrome.<sup>4</sup> These associated risk factors include hypertension, hypertriglyceridemia, low levels of high density lipoprotein cholesterol (HDL), abdominal obesity, insulin resistance and

type 2 diabetes mellitus (T2DM).<sup>5</sup> The prevalence of metabolic syndrome (MetS) is elevated to over 50% in the CHD population, more than double that of the general population.<sup>6</sup> Obesity and MetS further increases the risk of developing CHD through their association with small dense low-density lipoprotein (LDL) particles, systemic inflammation and abnormalities of fibrinolysis.<sup>7</sup>

Depending on severity, options for the treatment of obesity include behavioral weight loss counseling, exercise training and bariatric surgery.<sup>8</sup> Weight loss and exercise favorably affect a constellation of CHD risk factors which, in turn should positively affect overall prognosis. Indeed, significant weight loss achieved through bariatric surgery results in reduced overall and cardiovascular (CV) mortality.<sup>9–11</sup> Additionally, intentional weight loss achieved through behavioral modification in overweight individuals with coronary risk factors has been linked to a lower rate of development of CHD over a

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**Abbreviations and Acronyms**

BMI = Body mass index

BWL = Behavioral weight loss

CHD = Coronary heart disease

CR = Cardiac rehabilitation

CRP = C-reactive protein

CV = Cardiovascular

HDL = High-density lipoprotein

LDL = Low-density lipoprotein

MetS = Metabolic syndrome

PA = Physical activity

PAI-1 = Plasminogen activator inhibitor-1

T2DM = Type 2 diabetes mellitus

4 year follow up period.<sup>12</sup> For health care professionals caring for overweight individuals an understanding of the potential impact of weight loss is critical. The purpose of this review is to examine the deleterious consequence of excess adiposity, review the physiologic and metabolic effects of weight loss as they relate to prognosis, and to provide a review of the basic components of a behavioral weight loss (BWL) program.

quality of life both before, and after the onset of clinical CHD.<sup>20–22</sup>

### Insulin resistance/metabolic syndrome and type 2 diabetes mellitus

The insulin resistance/metabolic syndrome refers to a cluster of obesity-related metabolic factors that are closely linked to the development and progression of CHD.<sup>5</sup> The defining characteristics of MetS include centrally distributed adiposity manifest as a large waist circumference, impaired glucose metabolism, dyslipidemia and elevated blood pressure. Individuals with the MetS are at 3-fold increase risk for the development of CHD and stroke and are 5 times more likely to develop T2DM.<sup>23–25</sup> Intentional weight loss accomplished through diet and exercise is associated with improved insulin sensitivity and a decreased prevalence of the risk factors that constitute MetS and T2DM.<sup>26,27</sup> In the Finnish Diabetes Prevention Study<sup>28</sup> more than 500 obese subjects with impaired glucose tolerance were randomized to an exercise and caloric restriction intervention or a control group that received general dietary and activity counseling. Individuals were followed for a mean of 3.2 years for the onset of T2DM. In the intervention group, mean weight loss was 4.2 and 3.5 kg at years 1 and 2, respectively. Mean weight loss was 0.8 kg in the control group. Weight reduction in the intervention group was associated with a 58% reduction in the incidence of T2DM.

The Diabetes Prevention Program employed a similar exercise and dietary intervention along with the medication metformin to prevent or delay the development of T2DM.<sup>29</sup> Over 3,200 overweight subjects were randomized to an intensive program of caloric restriction and exercise, standard lifestyle recommendations plus metformin or the lifestyle recommendations plus placebo. Mean follow-up was 2.8 years. The group receiving the lifestyle intervention achieved a 5.6 kg weight loss and a 58% reduction in the incidence of T2DM compared to the placebo control group. The group that received the standard lifestyle recommendations plus metformin lost 2.1 kg and had a 31% reduction in the incidence of T2DM compared to controls. At the 10-year follow-up, despite partial weight regain, there remained a 34% decrease in the incidence of T2DM in the intensive lifestyle intervention and an 18% reduction in the metformin group compared to controls.<sup>30</sup>

The Look AHEAD (Action for HEalth in Diabetes) study is a randomized control trial comparing an intensive lifestyle intervention of dietary weight loss counseling and moderate exercise to enhanced usual care of T2DM on CV endpoints in over 5,000 overweight subjects with T2DM.<sup>31</sup> The Look AHEAD trial was terminated early after a mean follow up of 9.6 years, as it was determined that, despite achieving significant weight loss and fitness gains, the intervention did not significantly reduce long-term CV events compared to controls.<sup>32</sup> Look AHEAD, however, did demonstrate that overweight individuals with T2DM can achieve long-term weight loss success with a lifestyle intervention and a significant minority, 11% at one year and 7% at 4 years,

### Weight loss and coronary risk factors in the general population

Obesity has long been recognized as a marker of poor health due to its association with T2DM, CHD and mortality.<sup>13,14</sup> For nearly all obese individuals, weight loss is currently recommended for primary and secondary prevention of CHD.<sup>8,15</sup> Weight loss recommendations are made despite some evidence of an inverse relationship between overweight/obesity and mortality often termed the “obesity paradox”. The obesity paradox refers to the observation, derived mostly from retrospective observational database analyses, that overweight individuals may have more favorable health outcomes than do normal- or underweight subjects. This has been observed in diverse patient populations including individuals with CHD, hypertension, peripheral artery disease and heart failure.<sup>16</sup> Physiologic explanations remain somewhat elusive, although associations between low body weight and multiple chronic diseases with a poor prognosis such as chronic heart failure, cancer and arthritis are well known. One limitation of most studies reporting the existence of a paradoxical relationship between obesity and medical outcomes is the use of BMI as the measure of obesity.<sup>17</sup> Indeed, when alternative measures of body composition such as waist circumference are utilized the paradoxical relationship between total mortality and BMI is largely eliminated.<sup>18</sup> Thus, the obesity paradox has recently been termed a “BMI paradox”.<sup>19</sup> Nonetheless, it has been clearly demonstrated that intentional weight loss can favorably alter obesity-related risk factors for the development and progression of CHD. Few, if any, clinicians would argue against recommending weight loss for obese individuals with multiple obesity-related CHD risk factors such as is seen with the MetS. Certainly, BWL, which includes counseling and exercise, is also associated with an improvement of physical fitness, physical function and

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