Excess body weight in the form of adipose tissue is receiving a great deal of attention, given its profound detrimental implications for health and the burden it places upon the healthcare system. Body mass index (BMI) is perhaps the most commonly used measure for classifying subjects as either normal weight (18.5–24.9 kg/m²), overweight (25.0–29.9 kg/m²), or obese (≥30 kg/m²). While the BMI approach clearly has limitations, its general relationship to adiposity and ability to provide health/prognostic information warrants attention.

Current estimates indicate that over 67% of the adult population in the US is classified as being either overweight or obese with nearly 34% falling into the latter, more disconcerting, category. Figure 1 illustrates the dramatic rise in obesity in US adults from 1960 to 2008. From this figure, it is clear that the rise in individuals with excess body weight is primarily the result of growth in the obese population while the number of those classified as overweight has remained relatively stable.

Perhaps more troubling is the fact that the percentage of children (two to 19 years old) classified as overweight or obese in the US is nearly 32% (17% are obese). Lastly, the number of children aged two to 19 years who meet or exceed the 99th BMI percentile increased by 300% and 70% since the National Health and Nutrition Examination Surveys (NHANES) II (1976) and III (1994), respectively. Figure 2 illustrates the rise in obesity in US children from 1963 to 2008. Upward obesity trends are consistent across children of all ages.

Excess body weight and adiposity concerns are not limited to the US. In a recent analysis of 199 countries and territories, Finucane et al. estimated that nearly 1.5 billion adults worldwide are either overweight or obese by BMI criteria; 34% (502 million) are thought to have a BMI ≥30 kg/m². These estimates suggest one in three and one in nine adults worldwide are overweight or obese, respectively. The US had the highest BMI among high-income countries. Changes in BMI over the past several decades appear to be following an upward trajectory in most regions of the world, a troubling trend that has been labeled a ‘tsunami of obesity’ requiring immediate and substantial attention. If these trends continue, the World Health Organization (WHO) estimates that 2.3 billion adults will be overweight and more than 700 million of these individuals will be obese by 2015.

A primary concern over the dramatic increase in overweight/obesity prevalence is its clear link to increases in mortality, morbidity, and healthcare expenditure in the general population. Obesity is currently responsible for one death in 10 in the US. Recent data also indicate that,
Excess Body Weight and Coronary Artery Disease

Excess body weight is a primary contributor to the increased risk for coronary artery disease (CAD), as well as increasing the likelihood of developing other CAD risk factors. Moreover, once diagnosed with CAD, patients with excess body weight present with a poorer clinical profile in a number of respects. However, once an individual is diagnosed with CAD, there are data to indicate that excess body weight is associated with a reduced mortality risk, a phenomenon defined as the ‘obesity paradox’. The obesity paradox is, of course, counterintuitive and has caused some debate as to how patients with CAD who present with excess body weight should be counseled with respect to weight loss.11 This issue is particularly important for cardiac rehabilitation (CR), where excess body weight should be counseled with respect to weight loss.14 Recommendations for weight loss in patients with CAD.

One in three men and women in the US who are free of disease but obese at 40 years of age will develop CAD.2 The INTERHEART study, which assessed CAD risk in 52 countries, identified abdominal obesity as one of the nine key modifiable factors associated with elevated risk.9 A higher BMI in childhood (recorded between seven and 13 years of age) is also associated with an increased risk for coronary events in adulthood for both men and women.20 Cassidy et al.20 assessed change (mean follow-up 8.9 years) in coronary artery calcification in 443 asymptomatic individuals. Obesity parameters, including WC, the waist:hip ratio (WHR) and BMI were all positively associated with greater progression of coronary artery calcification in those subjects considered to be at low risk for CAD by the Framingham risk equation. An elevated BMI also substantially increases the likelihood of developing other traditional CAD risk factors such as HTN, T2DM, and dyslipidemia.12 In fact, the dramatic rise in the prevalence of T2DM in the US is paralleled by the rise in obesity.1 While the prevalence of other CAD risk factors has dramatically declined over the last several decades across all BMI categories, Gregg et al.22 reported that a diagnosis of HTN and T2DM still remains significantly higher in obese individuals. Moreover, obesity is associated with other detrimental factors such as cardiac remodeling, insulin resistance, increased...
systemic inflammation, a prothrombotic state and obstructive sleep apnea/sleep-disordered breathing. Thus, excess body weight and adiposity, particularly in the obese range, often precipitates, and then coexists with, a cluster of other risk factors that exponentially increase the likelihood of developing CAD. This clustering pattern of CAD risk factors, oftentimes led by obesity, clearly illustrates the importance of weight loss in preventing initial CAD events.

### The Detrimental Effects of Excess Body Weight in Patients with Coronary Artery Disease

Once a diagnosis of CAD is confirmed, the detrimental effects of excess body weight on a patient’s clinical profile continue. In a group of 415 males participating in CR, Binder et al. found subjects presenting with abdominal obesity (WC ≥102 cm; 50% of cohort met criteria) had a significantly higher prevalence of T2DM and HTN. Moreover, resting heart rate and triglycerides were significantly higher while high-density lipoprotein cholesterol (HDL-C) was significantly lower in subjects with abdominal obesity. In 2,273 subjects with T2DM and CAD, Albu et al. found excess body weight (assessed by BMI and WC) was significantly predictive of variables indicating increased atherothrombotic risk, including higher insulin, lipid, blood pressure, inflammatory, and procoagulation levels. Tani et al. found an increasing BMI was significantly associated with attenuated plaque regression over six months in 56 patients with CAD who were prescribed pravastatin. Perceived quality of life has also been found to be significantly lower, while the incidence of depression is significantly higher in patients with CAD who meet the criteria for obesity by BMI. Based on the currently available evidence, patients with CAD and excess body weight, particularly in the obese range, are likely to present with a host of characteristics that are consistent with poorer clinical status.

### The Obesity Paradox in Patients with Coronary Artery Disease

Although overweight and obese patients with CAD clearly demonstrate a number of factors consistent with poorer clinical presentation, there is rather compelling evidence that survival is improved in the higher BMI classes, a phenomenon termed the obesity paradox. Romero-Corral et al. conducted a meta-analysis in 2006 that included 40 studies, collectively including more than 250,000 patients with CAD. Patients with a BMI between 20 and 24.9 kg/m² were considered normal weight and the referent group for all survival analyses. Patients considered to have a low BMI (<20 kg/m²) had the highest risk for all-cause mortality, while overweight patients had the lowest risk. Obese (30–34.9 kg/m²) and severely obese (≥35.0 kg/m²) patients had no increased risk for all-cause mortality compared with the referent group. After adjusting for potential confounders (age, sex, and other CAD risk factors), overweight patients were at a higher risk for CAD mortality while overweight patients had a non-significant lower risk. Obese patients had no increased risk for CAD mortality while those with severe obesity were at significantly higher risk.

After controlling for potential confounders, overweight and obese post-PCI patients had a lower short-term (within 30 days) and long-term (up to five years) all-cause mortality compared with patients with a normal BMI. Overweight and obese post-CABG patients had significantly lower short-term mortality and similar long-term mortality compared with patients with a normal BMI. In 2009, Oreopoulos et al. assessed the prognosis of 31,021 patients with established CAD over a median follow-up time of 46 months. In the overall cohort, patients with a BMI <18.5 kg/m² had the highest mortality risk, while patients who were overweight (25.0–29.9 kg/m²) or Class I–III obesity (30.0 to >40 kg/m²: see Table 1) had the most favorable survival profile. Patients within the normal BMI range (18.5–24.9 kg/m²) had better survival than overweight patients, but were at a higher risk for mortality compared with those who were overweight or obese. Patients who were medically managed and classified as either overweight or Class I obesity (30.0–34.9 kg/m²: see Table 1) had a significantly lower mortality compared with patients with a normal BMI. Patients who were Class I obese and underwent CABG had the lowest mortality risk compared with other BMI subgroups. Patients undergoing PCI with Class II obesity (35.0–39.9 kg/m²: see Table 1) had the most favorable survival profile compared with other BMI subgroups. Lastly, patients in this study who were defined as

| Classification | BMI (kg/m²) | Disease Risk* Relative to Normal Weight and Waist Circumference |
|---------------|------------|-------------------------------------------------------------|
| Underweight   | <18.5      | –                                                           |
| Normal        | 18.5–24.9  | –                                                           |
| Overweight    | 25.0–29.9  | Increased                                                   |
| Obesity       | 30.0–34.9  | High                                                        |
|               | 35.0–39.9  | Very high                                                   |
| Extreme Obesity | ≥40        | Extremely high                                               |

*Disease risk for type 2 diabetes, hypertension and cardiovascular disease; *increased waist circumference can also be a marker for increased risk even in persons of normal weight.

BMI = body mass index.

Source: NHANES, 1998. 25

Table 1: Classification of Overweight and Obesity by Body Mass Index, Waist Circumference, and Associated Disease Risk

| Classification | BMI (kg/m²) | Disease Risk* Relative to Normal Weight and Waist Circumference |
|---------------|------------|-------------------------------------------------------------|
| Underweight   | <18.5      | –                                                           |
| Normal        | 18.5–24.9  | –                                                           |
| Overweight    | 25.0–29.9  | Increased                                                   |
| Obesity       | 30.0–34.9  | High                                                        |
|               | 35.0–39.9  | Very high                                                   |
| Extreme Obesity | ≥40        | Extremely high                                               |

*Disease risk for type 2 diabetes, hypertension and cardiovascular disease; *increased waist circumference can also be a marker for increased risk even in persons of normal weight.

BMI = body mass index.

Source: NHANES, 1998. 25
overweight or Class I/II obesity were younger and had a lower plaque burden but were more likely to undergo a revascularization procedure.

Several plausible explanations for the obesity paradox in CAD have been put forth. Previous investigations have consistently demonstrated that obese patients diagnosed with CAD present at a younger age with a lower plaque burden.30–34 These observations may indicate a referral bias where only the healthiest obese patients with lower disease severity are included in cohorts demonstrating the obesity paradox. The follow-up periods in the studies demonstrating improved survival with higher BMI may also be insufficient in length to capture the long-term negative consequences of obesity.29 There are limitations associated with quantifying adiposity by BMI, the primary clinical measure used to establish the obesity paradox in patients with CAD. For example, using a range of 18.5–24.9 kg/m² to define 'normal weight' may be too broad and the lower end of this classification may actually reflect unhealthy levels of decreased body mass. However, recent investigations have demonstrated the obesity paradox by both BMI and body fat, with higher body fat being an independent predictor of better survival.35–37

The associations between lean mass and BMI may also be an important explanatory mechanism for the obesity paradox.22 Patients at the lower end of, or below, the normal BMI range may have diminished lean mass, which is prognostically ominous, while in overweight and obese patients lean mass may be well preserved.29 To support this hypothesis, recent investigations have demonstrated that higher lean body mass was associated with better survival in patients with stable CAD, and lean mass independent of body fat in predicting survival.38–39 To this end, more accurate reflections of adiposity in particular problemmatic regions (i.e. abdominal obesity) may portray a different relationship between body mass and prognosis.40 For example, Cheng et al.41 found pro-atherogenic adipokines and pro-inflammatory tissue levels were significantly higher in abdominal adipose tissue compared with epicardial adipose tissue in a CAD cohort, indicating that patients with higher levels of abdominal adiposity were at greater risk. Bajaj et al.42 assessed the prognostic ability of both BMI and WC in 5,453 subjects being seen for management of CAD risk factors. Fifty-one per cent of males and 28.8 % of females had a previous diagnosis of CAD. A higher WC, but not a lower BMI, was a significant predictor of all-cause mortality. In 855 patients with CAD, Goel et al.43 found normal body mass defined by BMI and a high WHR (≥0.85 for women and ≥0.90 for men) were both predictive of increased mortality risk. Other investigations have also suggested WC or WHR measurements may provide a more accurate reflection of problematic (i.e. abdominal) adiposity and thus elevated risk.44–46 Lastly, the possibility that excess adipose tissue itself, reflected by a higher BMI, is protective cannot be discounted. Potential protective physiologic mechanisms of adipose tissue have been better elucidated in patients with heart failure.30–34 There is some evidence to indicate patients with a higher BMI have a higher metabolic reserve that may be protective against the deleterious effects of malnutrition.35–39 Such physiologic mechanisms may also exist in patients with CAD and preserved ventricular function, and research to better understand the obesity paradox should therefore continue. At this point in time, there is substantial evidence to indicate that patients with CAD who are overweight or obese by BMI have an improved prognosis. Therefore, the obesity paradox warrants clinical consideration in the CAD population.

Cardiac Rehabilitation—The Benefits of Improved Functional Capacity and Intentional Weight Loss

CR elicits dramatic positive benefits in patients with CAD.50 Improvements in functional capacity, blood pressure, lipid profile, systemic inflammation, insulin sensitivity, and quality of life are all well-documented outcomes following CR participation. Moreover, there is compelling evidence to indicate CR participation results in a significant risk reduction for all-cause and CAD mortality.51 A key CR benefit is the significant improvement in aerobic capacity. A convincing body of evidence indicates that aerobic capacity is one of the most important prognostic markers in apparently healthy individuals and virtually all patient populations.25 A recent meta-analysis by Kodama et al.,52 including 33 studies, 100,000 subjects, 6,000 all-cause mortality events, and 4,000 CAD events, assessed the prognostic value of aerobic capacity in apparently healthy subjects. The authors found that each one metabolic equivalent (MET) increase in aerobic capacity equated to 13 % and 15 % decreases in all-cause mortality and CAD events, respectively. Keteyian et al.53 assessed the prognostic value of peak aerobic capacity in 2,812 patients with CAD and found that each 1 mlO₂.kg⁻¹.min⁻¹ increase in peak oxygen consumption equated to an approximate 15 % decrease in mortality. The interaction between fitness and excess body weight has also received considerable attention in recent years.54–56 The prevailing message from these investigations indicates that higher fitness levels substantially decrease mortality risk irrespective of body habitus. In fact, Goel et al.57 found a non-significant trend toward increasing mortality risk in highly fit (peak oxygen consumption: male: ≥21.5 kg⁻¹.min⁻¹; female: ≥16.8 kg⁻¹.min⁻¹) CAD patients who were either overweight or obese by BMI compared with those classified as normal weight. In patients who were considered to have low fitness (peak oxygen consumption: male: <21.5 kg⁻¹.min⁻¹; female: <16.8 kg⁻¹.min⁻¹), those classified as obese had the most favorable prognosis while risk became progressively higher in subjects in the overweight and normal-weight BMI range. This study suggests a higher fitness level neutralizes or perhaps reverses the obesity paradox.

It is currently estimated that the percentage of subjects with CAD who are either overweight or obese is 80 % and 40 %, respectively.58 Current CR guidelines recommend the implementation of weight loss strategies in patients with a BMI ≥25 kg/m² and/or a WC >40 inches (102 cm) in men and >35 inches (88 cm) in women.59 Given the data supporting the obesity paradox in patients with established CAD, concern has been raised over weight loss in patients who are either overweight or obese.60 This is a somewhat disconcerting approach given the vast body of evidence clearly detailing the detrimental impact of excess body weight in the form of adipose tissue. The failure to distinguish between intentional and unintentional weight loss is a key limitation of the obesity paradox literature. Investigations establishing the obesity paradox have done so using cross-sectional assessments without tracking weight change over time and determining if those changes were beneficial or detrimental. It is plausible that subjects with a lower BMI had a poor prognosis because of unintentional loss of lean body mass, progressing toward or reaching a cachectic state.61 CR promotes intentional weight loss, which preserves lean tissue while reducing adiposity. Savage et al.62 assessed the impact of intentional weight loss in 15 overweight/obese patients with CAD who completed a four-month CR program. Body composition changes were assessed by dual-energy X-ray...
Risk

Table 2: Key Cardiac Rehabilitation Considerations in Patients Attempting Weight Loss

| Baseline Body Habitus and Caloric Expenditure Evaluation |
|--------------------------------------------------------|
| Assess weight, BMI, and waist circumference             |
| BMI ≥25 kg/m2 and/or waist >40 inches (102 cm) in males and >35 inches (88 cm) in females considered high and warrants weight loss consideration |
| Estimate resting caloric expenditure                     |

| Exercise Training Component |
|----------------------------|
| Aerobic exercise: Ideally 30–60 minutes per session; intensity should be between 50 and 85 % of maximal aerobic capacity; most, if not all, days of the week; exercise intensity ideally established from exercise testing at baseline |
| Resistance training: 8–10 different upper and lower body exercises (primarily multi-joint); 1–3 sets per exercise; 10–15 repetitions per set |
| Estimate caloric expenditure during exercise training    |

| Dietary Component |
|-------------------|
| Evaluate nutritional habits and provide guidance/education on strategies to improve healthy eating patterns as needed |
| Develop daily caloric intake recommendations |
| Ensure protein intake sufficient to preserve lean body mass |

| Overall Interventional Strategy |
|---------------------------------|
| Daily caloric deficit should be between 500 and 1,000 kcal/day |
| Attainment of caloric deficit primarily through exercise energy expenditure preferable to assist in preservation of lean body mass |

| Program Goals |
|----------------|
| Rate of weight loss should be 1–2 pounds per week |
| Reduce body weight by at least 5 % and ideally >10 % |
| Reduce circumference measurements into normal range |
| Maintain weight loss and circumference reductions long-term |

BMI = body mass index.

Currently available studies indicate that intentional weight loss through CR in patients with CAD who are overweight or obese appears safe and results in numerous health benefits. Therefore, recommendations for the implementation of intentional weight loss strategies in CAD patients identified as overweight or obese seem warranted and should continue. Moreover, improved fitness, a primary CR benefit, seems to neutralize or possibly reverse the benefits of excess body weight in patients with CAD. However, weight loss targets should perhaps be limited to the higher end of the normal BMI range (<23–24.9 kg/m²) given the greatest rise in adverse event risk appears to be in individuals approaching or dropping below the lower threshold of a normal BMI (<20 kg/m²). Patients who present with a normal BMI at the higher end of the normal range should be encouraged to maintain body weight. However, for CAD patients with a BMI ≤20 kg/m² upon entering CR, consideration should be given to the implementation of healthy weight gain strategies. In the current investigations examining intentional weight loss through CR, mean post-intervention BMI remained at the high end of the overweight classification (<29 kg/m²) despite dramatic improvements in a host of physiologic, functional, and psychological markers. Given realistic weight reductions in clinical practice are likely to follow these trends in weight loss, the likelihood of losing excessive body weight and compromising prognosis is extremely unlikely. If, in fact, excess body weight proves to be physiologically protective, weight loss through CR may provide the “best of both worlds”: numerous CR-derived benefits plus maintenance of a higher BMI. Abdominal adiposity should also be assessed by WC or the WHR. Abnormally high values for these measures have been shown to be prognostically ominous. In fact, higher than normal central obesity as determined by circumference measurements seems to indicate a worse prognosis, irrespective of fitness level.29,30 Therefore, the individually tailored CR program should heavily focus on reductions in central obesity when elevated. If a primary goal of CR for a specific patient is weight loss, the program should combine dietary and exercise interventions to elicit an appropriate negative caloric deficit.31–33 Efforts should be taken to ensure the preservation of lean body mass during weight loss. In addition to the benefits of exercise in preserving lean body mass, evidence suggests increased protein intake may be beneficial during the weight loss program.34–36 Table 2 lists key CR programming considerations when weight loss is a primary goal.37

Conclusions

Excess body weight, primarily in the form of adipose tissue, results in a host of adverse health consequences in patients not diagnosed with CAD. Moreover, excess body weight significantly increases the risk for CAD and mortality (through several mechanisms). Once an individual is diagnosed with CAD, excess body weight continues to lead to a negative health profile but is associated with improved survival, a phenomenon termed the obesity paradox. It is likely that reduced body weight in the overall CAD population reflects malnutrition and unintentional weight loss, leading to poor prognosis. Weight loss through CR is intentional, does not elicit a malnourished state, leads to a number of health benefits, and does not seem to lead to worsening prognosis. Therefore, unintentional weight loss and the obesity paradox and intentional weight loss through CR should be viewed as separate entities with very different outcomes. Therefore, weight loss interventions should continue in CAD patients with excess body weight who participate in CR.
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