

The Obesity Paradox. Intention of Making a Reasonable Suggestion for Secondary Prevention

To believe that we understand our world is both a pleasure and a sedative. Creativity to interpret the phenomenon is difficult to explain, such as the origin of the Universe, or 'simply' the sunrise or phases of the moon. In each historical and cultural period, they contributed to configure mythological or scientific models that provided a broad vision of reality. For part of the population, religions and –today– science fulfill this function: they are sympathetic interpretations of a complex reality, which allow us to live our lives with greater certainties.

In medicine, we also pose theories that help us focus on global health problems and make decisions for individual patients. We need simple truths that strengthen our operative thinking. When certain aspects of our experience or our explored reality do not match this model, we usually adopt –both individually and globally– two attitudes that often coexist: the first reaction is to ignore or deny the phenomenon, and when denial is already impossible, we look for a new explanatory model.

Something similar is happening to our concept of ideal body weight and diet.

Body weight, muscle mass, its fat component and its distribution seem to be simplified under the concept of “normality” and obesity. Similar to cholesterol and blood pressure models, body weight is thought as the equation “the more, the worse”, and thus we want to determine a hypothetical ideal weight.

We have no doubt that weight gain is associated with high blood pressure, diabetes, and cardiovascular disease, in addition to several metabolic disorders and other conditions. For that reason, cut-off points have been sought to define normal and excessive weight levels, and different obesity degrees, in addition to facilitate behaviors. The common definition uses the body mass index (BMI), which is calculated by dividing weight in kilograms by height in meters, squared. Thus, a person with 75 kg and 1.60 m height (165 lb and 5 feet) has a BMI of 29.3 (Table 1).

The association with cardiovascular risk is also verified with other obesity markers, such as waist-hip ratio (WHR) or waist circumference, which will be discussed later.

Within this concept, the finding that –in different contexts of the disease– patients with overweight or mild obesity grade I progress with less risk of death or new cardiovascular events than “normal” and slim patients causes a disruptive impact. The apparent protection of obesity is detected in follow-ups after an event or coronary surgery (post-infarction, angioplasty, coronary artery by-pass surgery) in chronic heart

Table 1. Categorization of obesity levels according to body mass index

Body mass index (kg/m ²)	Classification
< 18	Short - “Slim”
18 to 24.9	Normal
25 to 29.9	Overweight
30 to 34.9	Obesity I
35 to 39.9	Obesity II
> 40	Obesity III

failure, and after a stroke. This phenomenon has been called the obesity paradox.

This letter is intended to explore what we know about obesity in secondary prevention, in order to reiterate a wealth but systematically ignored information, and it will contribute to reflect upon the rationality of behaviors and discourses to patients.

RISK CURVES AND THE OBESITY PARADOX

The largest review on this topic considered 40 studies that involved 250,152 patients with coronary heart disease with a follow-up of 3.8 years. (1) For this analysis, curves about the relation between BMI and mortality were traced during the follow-up, corrected by multiple covariates. Considering the so-called normal individuals as control group, slim patients with BMI < 18 had increased all-cause and cardiovascular mortality. Overweight patients (25-29.9 BMI) had lower risk than normal patients. All-cause or cardiovascular mortality tended to be lower for obese patients (30-35 BMI), and even in the group with severe obesity (BMI ≥35), no increased all-cause mortality was observed.

To sum up: ***Slim people are at highest risk; then follow normal and very obese people, and the groups with better outcomes are those with overweight and moderate obesity.***

The reader may think I am making a mistake, or that there is something strange in this information. I will transcribe the graphics in order to describe them (Figure 1).

In Figure 1, which considers all the patients together, we find that taking normal BMI (> 18 to < 25) as risk index 1, the relative risk of slim subjects was 1.6 (ie, their risk was above 60%). Risk decreased with respect to normal subjects in overweight and obese patients. Severely obese patients reached the same risk as “normal” patients. This phenomenon is not homogeneous and is stressed in post-infarction

and post-angioplasty patients. After an angioplasty, whatever the obesity degree, the tendency is even a lower risk in obese patients than in normal patients!

Observing these curves, which include all the large series until 2006, and are repeated in the posterior ones, there is no doubt that the greatest progression risk in secondary prevention is focused on slim patients, and the second group at risk is the one with "normal" BMI.

A similar phenomenon has been observed in other diseases. For instance, in a study on 20,246 (2) patients who had ischemic stroke, with a 2.5 year follow-up, the adjusted risk for a new vascular event was 14% lower in overweight patients, and 16% lower in obese patients, compared with normal or slim subjects.

This observation is counterintuitive; the simple comment in a coronary care unit that this patient's long-term prognosis concerns because he/she is slim causes disbelief and even compassion. In medicine, it surprises to see how what is not understood or cannot be incorporated into a coherent bunch of ideas simply becomes invisible or nonexistent.

The obesity paradox questions the recommendations about diet and weight loss in patients with cardiovascular disease, and has given rise to an active debate trying to understand the implicit message.

We will review the main explanatory hypotheses of these observations, and then discuss up to what extent these findings may influence behaviors with the individual patient.

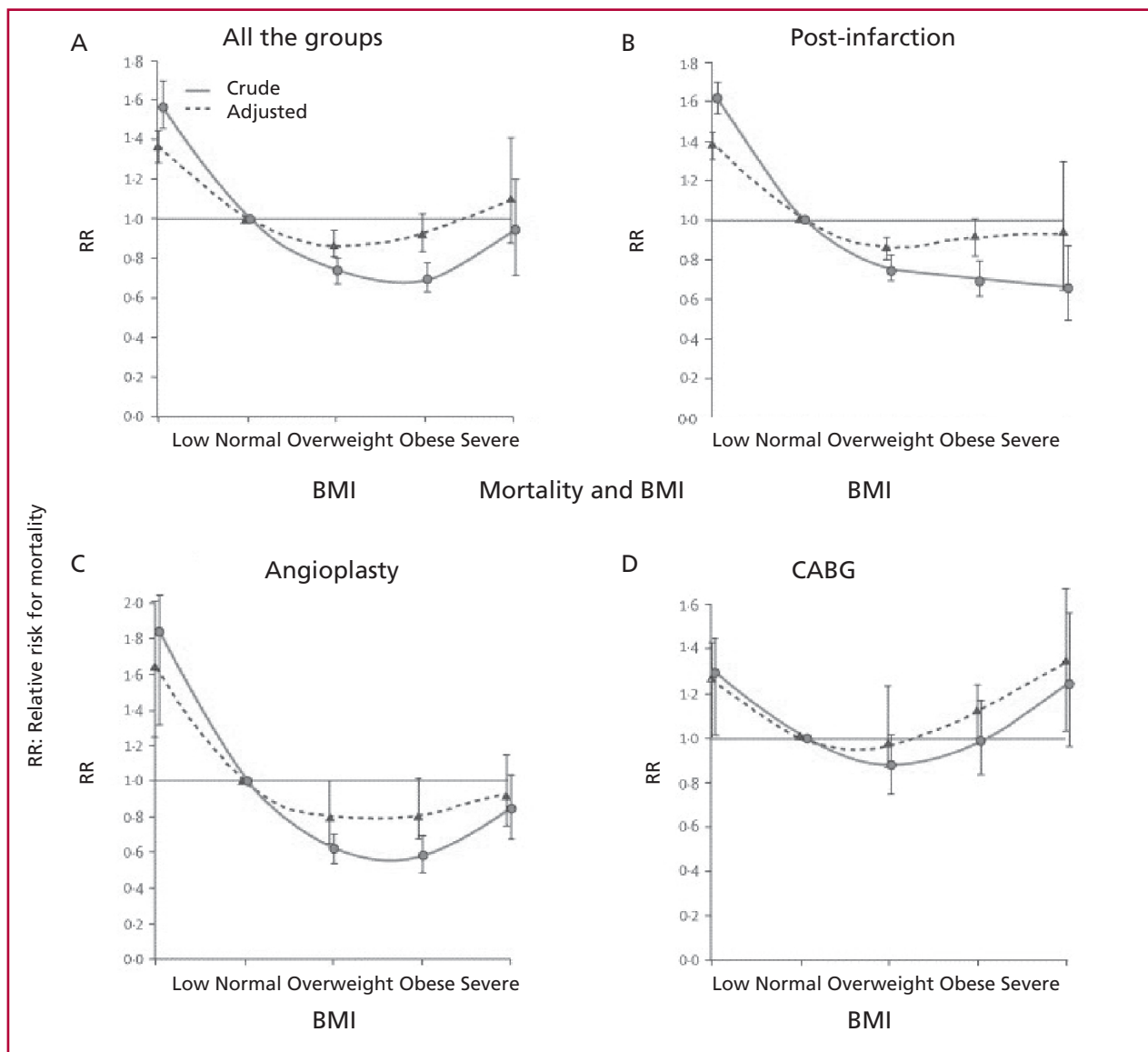


Fig. 1. Relation between the weight categories used in Table 1 and the all-cause mortality risk at 3.8 years of follow-up in more than 250,000 patients with coronary heart disease. The normal group (18-24.9 BMI) was considered as relative risk 1. Crude risk is expressed by continuous line, and risk adjusted by age, by dotted line. Modified from cite 1.

FINDING AN EXPLANATION TO THE CORONARY ARTERY DISEASE PARADOX

Explanation 1: Inadequate understanding of confounding factors

The phenomenon of risk factors and acute infarction mortality

Epidemiology shows us that the association between variables does not indicate causality or mechanisms. For instance, some years ago, the implication of smoking in acute and long-term outcomes of infarction was largely discussed. It was observed that patients who smoked and had acute myocardial infarction presented lower intrahospital mortality rate.

This information caused confusion with the role of smoking. How come such a documented and aggressive risk factor might be protective in another aspect?

A deeper analysis showed a very strong confounding variable: age. Smokers who have a myocardial infarction are 10-15 years younger than non-smokers. Since infarction mortality rate is related to age, when smoking was statistically corrected for each age group, it lost its "protective" role during the acute phase.

This smoking paradox about the acute evolution is also reproduced for the AMI and all the remaining risk factors in a very singular way. In a recent study, in-hospital mortality was lower when the number of risk factors was higher, considering the history of hypertension, dyslipidemia, smoking, diabetes, and family history of coronary artery disease. (3) As seen in Figure 2, mortality was four times higher in patients with no risk factors (14.9%) than in those in whom the five factors were considered (3.6%). The best explanation for this apparent paradox is that risk factors advance the development of coronary heart disease, and that myocardial infarction in hospitalized patients presents a higher mortality rate with age. In fact, there was a difference of 14 years in the mean age of patients with no risk factors, 71.9 years, as opposed to 56.8 years with five factors. Correcting by age and other variables, the relative risk between both of them is no longer 4 times but 1.6 times, ie, a 60% higher. There are probably other variables not considered in the model, that is, other "confounders", besides age or those considered in the analysis, which might explain the observation.

The same phenomenon occurs with BMI and acute evolution: the slimmest patients are much older than those of greater weight, and the explanation in this regard may just be that there are several unrecognized confounding factors. Will this explanation, which works very well for acute evolution, be the solution of the obesity paradox enigma at long-term follow-up?

The control of risk factors and late mortality after an infarction

The problem of risk factors and their influence on long-term follow-up is quite different. In the case of myocardial infarction, it is transformed when follow-

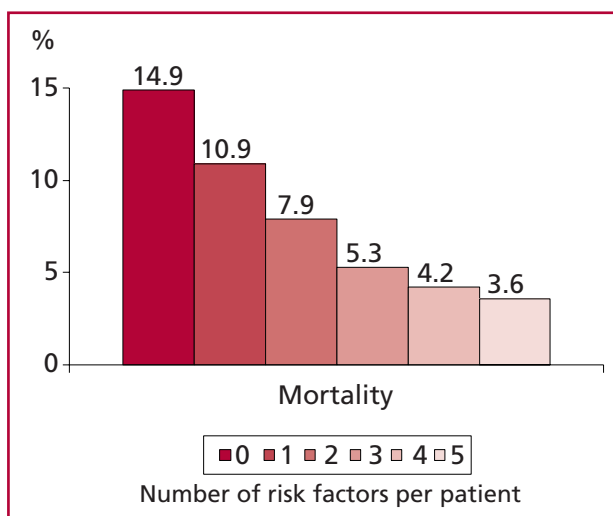


Fig. 2. Relation between the number of risk factors as antecedent and the mortality risk during hospital stay in 542,008 patients from the National Registry of Myocardial Infarction. (3)

up is considered after the infarction. Subjects who do not give up their smoking habit have their cholesterol levels high, or increased risk during follow-up, ie, those factors still imply risk for a worse long-term outcomes if they are not improved.

When dealing with BMI and obesity, the role of confounders, and particularly age, may be a good explanation to acute evolution, but it is not enough to explain the long-term outcomes, at least conceptually. We have no validated treatment to reduce stable weight both in primary and secondary prevention, and BMI is not usually changed in the series follow-up, as opposed to common risk factors. Despite BMI does not change, the greater the weight and the initial BMI, the lower the progression risk is.

In clinical practice, it is very difficult to achieve a stable weight reduction, which may be illustrated with the results of the Courage study. (4) The trial enrolled 2,287 chronic coronary patients to assess the role of angioplasty under an optimal medical treatment. Regarding baseline values, which were quite acceptable, they achieved significant reductions of cholesterol levels, blood pressure, and smoking, which were stable during the five years of follow-up. Moreover, they managed to increase the hours of weekly exercise and changes in the diet, but they had no effect on body weight. Initial BMI of 28.7 ± 0.18 slightly increased to 9.0 ± 0.21 at five years, both in patients with angioplasty and in those under medical treatment. Cardiologists will accept that this is very similar to what we usually observe at our offices about what we can or cannot achieve with our patients.

Despite the many statistical treatments, the paradoxical association between body mass index and mortality rate could not be corrected by confounding factors.

Explanation 2: Body mass index is a poor discriminator of fat percentage by weight.

In the review by Canto et al (3) discussed above, the authors arrived at the following conclusion: "The better outcomes for cardiovascular and total mortality seen in overweight and mildly obese groups could not be explained by adjustment for confounding factors. These findings could be explained by the lack of discriminatory power of BMI to differentiate between body and lean mass."

This is a very interesting hypothesis: there are people with more weight at the expense of muscle mass, and others with less weight but higher proportion of fat weight. Hypothetically, the proportion of fat by weight would be the risk message.

This argument is sustained by several epidemiological series on healthy population. A J-curve behavior according to their BMI was observed in a study on 787 male subjects with a 22 year-follow-up. (5) Fat percentage by weight and lean mass were also calculated, and the J-curve disappeared with that correction: the risk was a linear increasing function when the percentage of fat mass was higher. Divided by fifths, the highest fifth of percentage fat mass presented a mortality rate 40% higher than men belonging to the lowest fifth.

However, this does not seem to be the explanation for coronary patients, and it was disproved by a detailed prospective study, in which the body fat percentage was calculated by measuring the skin folds and their distribution. (6) In this series, body fat composition was defined as high when it was > 25% in men and > 35% in women. During the 3 years of follow-up, patients with low body composition presented with a higher mortality rate, regardless of their BMI. The group with low body fat composition and low BMI presented with a mortality rate of 11% vs less than 4% in the other three groups. The odds ratio for increased risk was 4.25 (CI 1.76-10.23). That is, chance of death was four times higher for the slimmer group with lower proportion of body fat composition. **Obviously, the problem of the paradox is not explained by the fat percentage by weight.**

Explanation 3: After diagnosing the disease, overweight patients improve their risk with their treatment, even without changing their weight, much more than normal weight or slim patients.

Weight gain is associated with development of hypertension, dyslipidemia, and diabetes, and a large proportion of the associated risk is explained by those factors. A hypothesis which might explain better long-term outcomes is that, today, both blood pressure and dyslipidemia can be managed with medication even if body weight does not change. A valuable observation in this regard was provided by the publication of a large cohort study on patients in Holland after a coronary angioplasty. (7) First of all, in their 6,332 patients, whose average follow-up time

was 6.1 years, they demonstrated a lower long-term mortality in overweight and obese patients (25% and 28% respectively) than in those with "normal" weight, confirming the curves reported above and represented in Figure 1.

The interesting point in this trial was that a more optimal medical treatment in the obese group than in the normal group was observed: 85% vs 75%, respectively. Optimal treatment was defined as the use of at least three of the four types of medication known to reduce long-term mortality: aspirin, statins, ACE inhibitors, and beta-blockers. Adherence to treatment was associated with better prognosis, and the multivariate analysis showed that taking into account adherence, BMI association with prognosis was no longer significant.

This study suggests that the evolutive difference between obese and normal patients after angioplasty is mediated by the adherence to recommended treatment measures, ie, by a different behavior to comply with the secondary prevention guidelines.

A nother form of analyzing the topic in the same vein is that the influence of obesity on risk may largely be stopped by controlling blood pressure and cholesterol. Genetic or unrecognized factors that would remain unchanged may influence on slimmer patients, maintaining their spontaneous tendency to new events.

Explanation 4: Body fat distribution is more important than its absolute magnitude, and would reveal the true message of obesity risk.

Body fat distribution is related to cardiovascular risk, regardless of BMI. "Apple-shaped" fat distribution (higher waist circumference and higher waist-hip ratio), called androgynous obesity, is associated with higher cardiovascular risk than "pear-shaped" distribution. In the latter, called gynoid obesity –with higher hip circumference and lower WHR –, the risk is much lower. The INTERHEART study showed that increased WHR had a stronger correlation with myocardial infarction than BMI, and that it further discriminated risk groups. (8)

The IDEA study (9) measured the heap circumference and the weight and BMI in 160,000 individuals in primary care consultation. A correlation between both parameters, and the presence of diabetes or cardiovascular disease were observed, with a better contribution of waist circumference, corrected by the BMI. Thus, in patients with no apparent overweight, increased abdominal circumference was associated with diabetes and heart diseases.

Visceral obesity versus subcutaneous obesity

There are several hypotheses to explain this phenomenon, given the complex metabolic and hormonal activity of adipocytes, which is quite different in perivisceral fat than in subcutaneous fat.

In a pathophysiological publication, Mc Carty (10) argues to have solved the paradox: "peripheral" obesity (less abdomen, more hip) would be effective due to a number of characteristics of these adipocytes (increased lipoprotein lipase activity, different levels of adiponectin production and, therefore, differences in its anti-inflammatory effect on insuline resistance and progression of atherosclerosis). Adiponectin, a hormone secreted by fat tissue and with anti-inflammatory and anti-atherogenic benefits, is reduced in obese patients, but particularly in those with androgynous distribution. (11)

This hypothesis was assessed in a recent meta-analysis. The authors investigated the prognostic value of BMI after an acute coronary event, and the so-called central obesity, taking into account the WHR or the abdominal circumference. Four published trials were included, together with a series by the Mayo Clinic. (12) Of a total of 15,923 subjects, whose individual data were obtained from the databases, in a follow-up median of 2.3 years, it was observed that a higher WHR improved by the BMI was associated with increased mortality. Dividing the WHR into tertiles, in the upper tertile with respect to the lower one, mortality rate was 70% higher in the normal BMI group and 93% higher in the obese group. BMI was inversely associated with mortality in this study.

The explicit message of this study is that central obesity is a risk factor for increased mortality, which would in part explain the poor prognostic role of BMI with respect to WHR.

May the difference between prominent abdomen and bulging hips explain the paradox?

Personally, I believe that this explanation cannot solve the obesity paradox, for several logical reasons:

- a) The only way to explain the paradox would be that the greater the overweight, the larger the hip circumference rather than the abdominal circumference, and that precisely the peripheral fat would have a positive effect. However, in this study, subjects with higher BMI were associated with higher WHR and waist circumference values.
- b) If this effect existed, progress curves in healthy subjects should not have to be different from those in subjects after a cardiovascular event.
- c) In this study, tertiles of waist-hip circumference were not reported in a non-adjusted way to BMI. Given that waist grows more than hip in case of greater weight in the average of the study population, the circumference was presumably not associated with higher risk on the univariate analysis, and ***I would assume that, in fact, it had the same behavior as the BMI: the longer the abdominal circumference, the lower the progression risk, without carrying out a statistical adjustment.*** Its association with higher risk was only evident when improving by BMI. To clarify this point: criteria to divide the waist circumference into tertiles in slim male

subjects were 84 and 90 cm (33 and 35 inches). In obese patients, tertile cut-off points were 107 y 115 cm (42 and 45 inches). The risk of having a waist circumference longer than 90 cm (35 inches) when BMI is normal is much higher than having 107 cm (42 inches) if BMI is elevated. Clearly, there is no common value to stratify by waist circumference or BMI; it only gets value when BMI is considered.

In an editorial (13) with a very expressive title – *Excess visceral adipose tissue/ectopic fat: the missing link in the obesity paradox?*–, the author supports this concept, but explains that there is no abdominal circumference value or WHR that can be considered independently of BMI, ie, the level of body weight.

Explanation 5: The association between obesity, cardiovascular risk and mortality is not similar in different age/risk groups, and it is misunderstood.

We have accepted that greater weight is associated with hypertension, diabetes, and cardiovascular disease at younger ages in healthy populations. However, the influence is not homogeneous and may vary for different age groups.

In the classic review that summarizes the influence of BMI on the long-term outcomes, in 900,000 adult individuals included in prospective studies, (14) it is clearly confirmed that the risk for death is lower in the group with BMI of 22-25. Figure 3 also shows the J-shaped behavior, with higher risk for progressive death in slim (BMI < 18) and obese individuals, with a small difference in overweight subjects. For example, a very high BMI (over 36) is required to match the risk for low-weight subjects (BMI 16). This behavior is similar in women, but with a lower risk for death per year in each category compared with men, and it is adjusted for age.

Considering a BMI of 22.5 to 25 as optimal, projections are that survival in middle-aged adults with a BMI of 30-35 will be reduced by 2 to 4 years, and in the group with a BMI of 40-45, by 8 to 10 years.

In 2010, a new analysis including 1.46 million adults with very similar curves was published. Globally, risk was lower with a BMI of 22.5 to 25. (15) These outcomes are summarized in Figure 4.

Body mass index, elderly, and cardiovascular risk

The ideal BMI level changes with age. Figure 5 shows that, at older age, the peak-off that indicates lower mortality risk moves to higher BMI, matching the categories of overweight or obesity I in comparison with the slim subjects and even with the so-called normal weight subjects. (16)

In classical series, in subjects over 70 years of age, the ideal BMI corrected by a number of variables is 30-32, that is, at the level of obesity I. (17) In a more recent series in Spain on 1,008 individuals over 65 years of age with a follow-up of 11.6 (8), the ideal BMI was between 30-35, that is, obesity I. Mean survival rate in obese I subjects was 13.8 years; in overweight

subjects, 12.3 years; in normal weight subjects, 10 years; and in the slim ones, 5.6 years. In this age group, obese subjects survived, on average, almost four years longer than “normal” subjects.

The curves of the relation between BMI and mortality in coronary patients are almost identical to those of older age groups.

DOES OBESITY PARADOX CHANGE DIETARY RECOMMENDATIONS? EVIDENCES AND DIET

A few weeks ago, a 65-year-old patient came for consultation; he had been implanted a drug-eluting

stent due to an asymptomatic lesion of the anterior descending artery. He is 1.78 m (5.84 ft) high and weights 81 kg (179 pounds); his blood pressure is normal, but his LDL cholesterol is very low; he is a non-smoker and does physical activity. He lives in fear of a possible disease progression, which was always asymptomatic. He went to another doctor, who recommended him to lose those “7 extra pounds”; he has tried on several occasions, but found it difficult to achieve.

Are there evidences for this suggestion? Or perhaps a better question would be if there are evidences of clinical benefit with a low-fat diet or a diet aimed at weight loss, or a weight change induced by doctors for coronary patients, which would have shown a positive effect.

The answer is NO.

Low-fat diet

After a myocardial infarction, for instance, patients are recommended a low-fat diet and weight loss if they belong to the overweight or obese groups.

Low-fat diet has been prospectively assessed in several trials with systematically negative outcomes. In a meta-analysis, relative risk reduction was 6% (CI 6 a +16%), which was not significant. (19) Afterwards, the DART trial on diet reported a 10-year follow up. (20) The advice of following a low-fat diet had little adherence and was not associated with mortality reduction. In this same trial, the addition of fish oil was related with a significant reduction of mortality rate.

Low-fat diet in primary prevention has been assessed on women in a large trial. (21) A total of

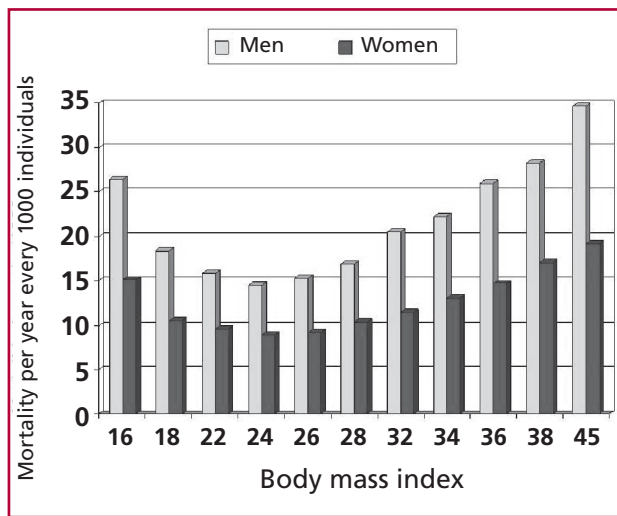


Fig. 3. Risk for death in adults according to BMI adjusted for age in each sex. A J- or U-curve behavior with the off-peak risk in the 22-24 BMI segment is observed. Data taken from the Prospective Studies Collaboration.

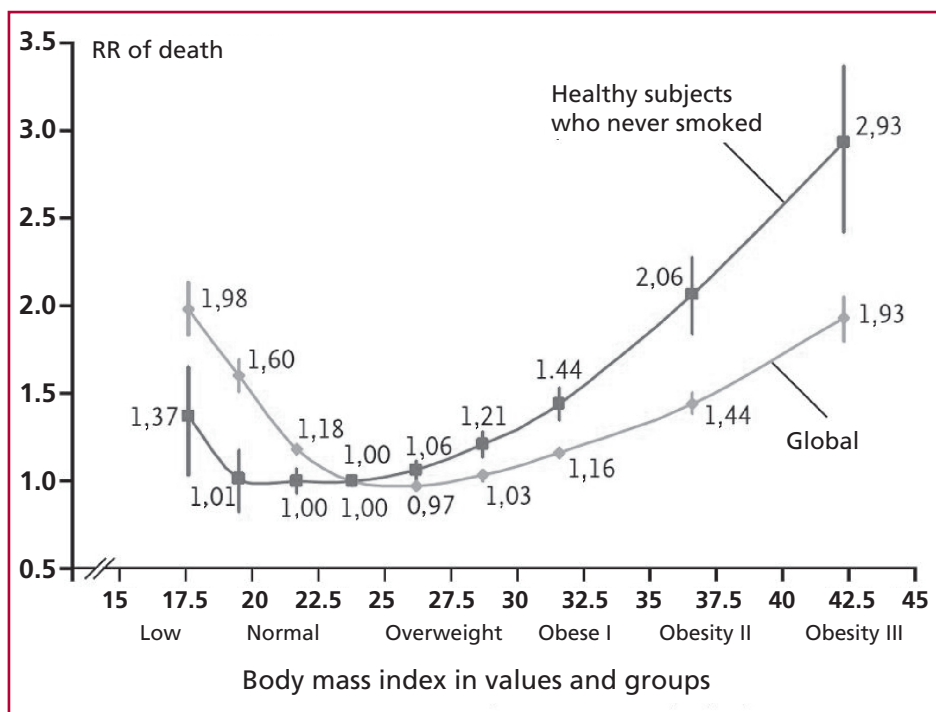


Fig. 4. Relation between BMI and progressive mortality. In the overall population, it is observed that there is little difference of risk with BMI between 22.4 and 32.5; risk increases with a BMI over 35 (RR 1.44) or below 20 (RR 1.60). If non-smokers are considered, the curve is similar to Figure 3. (15)

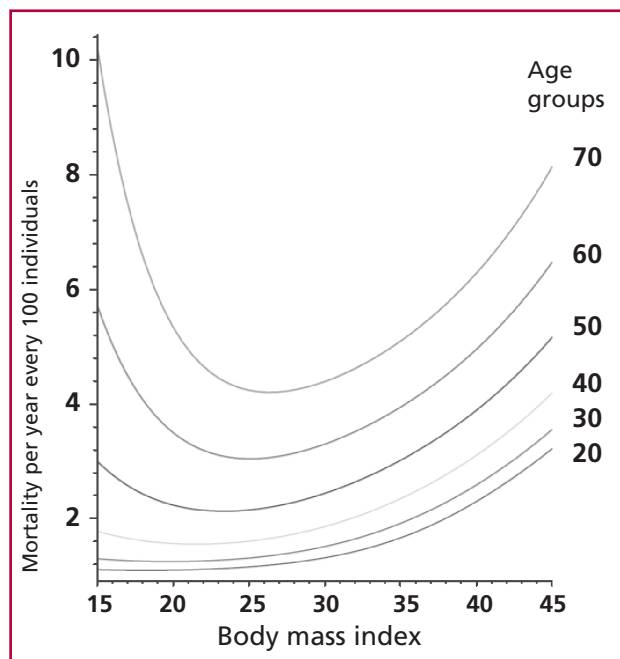


Fig. 5. Relation between mortality, expressed in deaths every 100 individuals, and BMI for different age groups. It shows a migration of the nadir of risk for middle-aged subjects close to 22-25 towards 28-30 BMI in older groups. (16)

48,835 postmenopausal women were included, who ate more than 30% calories as fat (35% on average), and reduced this percentage to an average of 28%. The study lasted for five years, with a high rate of adherence to diet. On average, 1kg (2.2 pounds) weight was lost with the low-fat diet, lipid levels were not substantially changed, and there was no effect on morbidity and mortality. The obvious conclusion of this study is that the current recommendation in the United States about the expected proportion of calories favoring carbohydrates or proteins with respect to fat, even when followed, *does not exert beneficial effects on health.*

The few dietary recommendations based on evidence we have are focused on Mediterranean diet, rich in olive oil, fruit, nuts, which is not intended to weight loss.

Evidences about weight loss

Studies on weight reduction in general

In patients controlled by series for long periods of time on different occasions, general progressive weight loss, in the absence of apparent conditions that motivate them, is associated with increased progressive mortality. This decrease does not discriminate between intentional or unintentional reductions.

As an example, a study carried out in Malmo, Sweden, included 5,722 subjects with no apparent conditions who were screened twice every 6 years, comparing BMI progress and further clinical evolution during 16 years. Cancer mortality and deaths during the first year after the second screening

were excluded to avoid confounding factors. Subjects who –on average– reduced their BMI in at least one point in ten years (equivalent to 4 kg, approximately) had an increased mortality risk that, according to the baseline BMI group, varied from 1.4 to 2.6 times, ie, 40% to 160%. It also increased in those subjects who increased their BMI if they were already obese. Taking into account non-smokers, obese subjects had a greater mortality rate when they lost weight than when they remained stable. For researchers, weight loss was associated with greater progression risk, which was more marked in obese non-smokers. (22)

Other studies have confirmed the same observation: progressive weight loss or fluctuation are associated with greater risk. In a cohort of 8,479 patients of the NHANES-I study (23), it was reported that risk was 83% higher (CI 25-170%) in those who had BMI fluctuation. Increased mortality was also seen in the weight loss group (RR 3.36; CI 2.5 - 4.5), compared with the stable obese group.

These observations have a very important bias, since it associates, in the same group the intentional weight loss aiming at preventing, with the unintended loss related to unknown factors or underlying or inapparent conditions.

Even more interesting is to evaluate the effect of weight loss in those who voluntarily try using different methods.

What would happen if patients “took heed” and lost weight? Intentional reduction

We cannot but speculate about this answer, but in our imagination, we guess they would have better outcomes. On the basis of short-range trials, we can expect that control of blood pressure, cholesterol and glycemia be facilitated.

We lack this information from patients with coronary artery disease, but there are many epidemiological series that have assessed the intentional weight reduction and the contribution to weight loss on mortality risk.

In the first place, the outcome is different in subjects who take the decision of losing weight on their own from those who are clinically indicated to do so. A research study of 4,896 individuals aged 56 to 75 years analyzed unintentional and intentional weight loss, and for the latter, its underlying reasons. (24) In the first place, it was confirmed that unintentional weight loss was associated with a 71% increase in mortality risk. Those who lost weight intentionally presented heterogeneous behaviors: in those who lost weight for personal reasons, mortality risk decreased by 41% at the expense of cardiovascular diseases. In those who lost weight due to clinical advice or certain health conditions, mortality risk increased 37%.

Another cohort study (25) of 2,957 healthy adult participants with BMI > 25 analyzed the intention to lose weight and its relation to long-term outcomes. In this group, those losing weight had an increased

mortality risk of 86% compared with those with stable weight, and even with those gaining weight. The authors' conclusion is that deliberate weight loss in overweight individuals without co-morbidities may be hazardous in the long term progression.

In a meta-analysis (26) of 26 trials that assessed the effect of intentional weight loss in obese subjects with no associated conditions, intentional weight loss had a neutral effect on all-cause mortality, RR 1.01. Unintentional weight loss was associated with excessed risk of 22 to 39%. In obese individuals classified as unhealthy –affected by obesity-related conditions–, weight loss had a small benefit on mortality, 16% (3-27%), but in overweight patients, even with related conditions, mortality increased by 9% (2-17%). As we see, the possible beneficial effect of intentional weight loss is, at best, small, with variations according to the degree of initial BMI, presence of conditions, and unconvincing behavior in subgroups.

Effects of weight reduction after a coronary event

There are virtually no trials that have assessed the usefulness of weight loss after a myocardial infarction on an adequate number of patients in order to draw a conclusion. The problem lies in that there is no effective treatment to achieve weight loss of some magnitude, except for bariatric surgery.

Over the past decade, two large trials with dietary interventions were planned; one of them mainly on patients with cardiovascular history, and the other one on diabetic subjects.

The SCOUT trial (27) enrolled 10,744 subjects with a history of cardiovascular disease (68%) and/or diabetes, with a BMI between 27 and 45. Mean BMI was 33, mean waist circumference was 114 cm (3.74 ft) in men, and 109 cm (3.58 ft) in women, and an a mean weight of 97 kg (214 pounds). All the patients participated in a diet and check-up program, and one of the two groups received sibutramine. The mean weight loss during the lead-in period was 1.9 kg in the placebo group and 4.3 kg in the sibutramine group. The difference in favor of the drug was a mean of 2.4 kg, with a follow-up of 3.4 years. Despite weight reduction, sibutramine was associated with higher pulse rate (mean 3 beats), higher blood pressure (1 mm Hg), and increased risk of nonfatal myocardial infarction and nonfatal stroke, all of which led to stop the trial. There were no differences in all-cause or cardiovascular mortality.

This trial also shows the limitations of our current interventions to manage weight reduction. We lack validated drugs, except for orlistat. Dietary intervention in a trial with several check-ups led to a weight reduction of only 1.7 kg in the placebo group. The greatest reduction with sibutramine, ranging from the best that can be achieved through diet in controlled studies, had no positive but harmful impact, perhaps antagonized by its adverse cardiovascular

effects, although they were very modest.

The second trial, Look Ahead Trial, (28), prospectively enrolled 5,145 overweight or obese patients, 59.5% women with a mean age of 58.7 years, and type 2 diabetes. Usual treatment was compared with dietary recommendations and drugs, with an intensive intervention –frequent exercise, group meetings, provision of diets, and more frequent checks. The trial is designed for a 13-year follow-up, and the first outcomes at 4 years have been reported. Intensive intervention was associated with weight loss (6% body weight vs 1% in the control group), improvements in fitness, and reduction in systolic (2.3 mm Hg) and diastolic (0.5 mm Hg) blood pressure and in glycosylated hemoglobin levels (0.36% vs 0.09% in the control group). Surprisingly, LDL cholesterol levels were lower in the control group owing to greater use of statins. These effects were not reflected in the clinical outcomes during the first 4 years, and long-term outcomes will be necessary to estimate the possible benefit.

The effect of weight on the progress will be difficult to isolate from other variables such as fitness, which is greater in the intensive intervention group. In patients with coronary artery disease, the usefulness of cardiac rehabilitation is well consolidated, (29) with 20% reduction of all-cause mortality and 27% of cardiovascular mortality.

FINAL COMMENT: DIETARY RECOMMENDATIONS AND EVIDENCES

We have only a few useful tools to support our strategy focused on weight reduction, and even worse, we cannot even confirm that if we succeeded we would have some benefit. *It is impossible to imagine that weight loss may be achieved at no price on behavioral, pharmacological and lifestyle changes, whose final outcome should be assessed in large trials.*

Population evidences indicate that most of the patients who visit a cardiologist –the elderly, or subjects with established cardiovascular disease, overweight or with obesity I– do not have, in the worst case, a higher risk than normal subjects, and always have a lower risk than slim subjects. We have discussed how difficult it is to draw a practical conclusion from this observation, which leads to several and conflicting interpretations. However, there is no doubt that it weakens our conviction about the model of interpreting “ideal” body weight and its relation with prognosis in coronary patients.

In an effort to project this abundant epidemiological, clinical, and pathophysiological information onto the office practice, perhaps the conclusion is simple.

In secondary prevention, we have strong evidences about the benefit of pharmacological interventions (aspirin, statins, beta-blockers, and ACE inhibitors, particularly for ventricular dysfunction) or non-pharmacological interventions (eg. exercise in rehabilitation programs) on mortality rate.

In this context, we have no clinical evidence of

the benefits of reducing fats in the diet or trying to lose weight in any of the BMI groups. Even some epidemiological observations are oriented in the opposite direction.

I think we should humbly provide this information to our patients: we do not know if weight loss will improve their clinical prognosis, or how to achieve it, we do not know if eating less fat is of any use, and the little we know suggests moving to a Mediterranean type of diet, ie, more fish, fruit, nuts, and olive oil. In certain contexts, such as cases of parameters which are difficult to manage with pharmacological strategies (hypertension, dyslipidemia, and glycemia), weight loss is already a therapeutic indication with a specific goal, and justifies the huge effort and the required cultural change.

Perhaps, the recommendations we keep on repeating senselessly have their root in less scientific domains. We should not forget that the etymological origin of "obese" is "eating a lot", and that gluttony has been considered a cardinal sin. Obesity is still attached to its stigma of sinful behavior, a personal failure that unables to repress harmful passions, a behavior that deserves some kind of punishment, and part of these concepts are still included in the thoughtless speech about the importance of losing "those 7 extra pounds".*

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* I sadly remember Romina Yan, the Argentinian young actress who died suddenly after several hours of vigorous exercise and was following a restrictive low-calorie diet which was associated with potassium deficiency. On the days that followed her death, cardiologists started to recite the creed about the importance of preventing sudden death in young women, precisely recommending the causal factors for this case, at least in my opinion: the systematic recommendation of having an "ideal" weight and aerobic fitness. They forgot that, among vulnerable and highly exposed people, this situation leads to extremes such as anorexia and bigorexia, which could lead to death.

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