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Obesity and the future. New problems and new solutions

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Obesity is, nowadays, a major health problem for all countries due to its increasing prevalence and its substantial implication in health for chronic disease and mortality. The worldwide prevalence of obesity nearly doubled in the last three decades. According to data from the National Health and Nutrition Examination Survey (NHANES), 35.7% of American adults are obese and 17% of children and adolescents aged 2-19 years are obese. In Europe over 50% are overweight and around 23% are obese. In 2006/07, the percentage of the Spanish obese population situated at 15.5% among men and 15.2% among women. This prevalence rose to 22.9% in 2010.¹

Obesity is a multifactorial chronic disease whose etiology is an imbalance between the energy ingested in food and the energy expended. This imbalance is promoted by complex interactions among inadequate dietary habits, diminished physical exercise and genetic background.² The excess energy is stored in fat cells that enlarge and/or increase in number. This fact leads to an adipose tissue dysfunction, the pathological lesion of obesity, whose consequence is the development of other diseases, such as diabetes mellitus, heart disease, neurological disease and some forms of cancer³ (Fig. 1). Obesity is instrumental in the development of type 2 diabetes mellitus and abdominal obesity was strongly associated with cardiovascular disease and diabetes, even in patients lean by body mass index as demonstrated by recent data generated during the International Day for the Evaluation of Abdominal obesity (IDEA) study in Spain.⁴ In addition to the widely known relationship between obesity and cardiovascular disease and diabetes

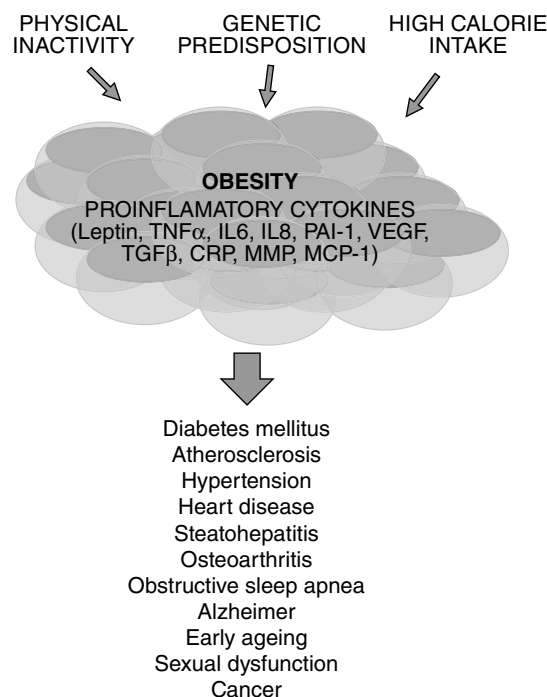


Figure 1 Health-related problems produced by an excess of body weight. CRP: C-reactive protein; IL: interleukin; MCP-1: monocyte chemoattractant protein-1; MMP: matrix metalloproteinases; PAI-1: plasminogen activator inhibitor-1; TGF- β : transforming growth factor- β ; TNF- α : tumor necrosis factor- α ; VEGF: vascular endothelial growth factor.

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mellitus, obesity itself is considered the second leading avoidable cause of cancer, after smoking. Approximately 5% of cancer may be attributable to excess weight and 15%-20% of all cancer-related deaths in subjects aged ≥ 50 years might be attributable to obesity.⁵ In fact, it was recently corroborated in a homogeneous population from Spain that overweight/obesity is significantly more prevalent in post-menopausal breast cancer patients.⁶ In fact, the prevalence of overweight and obesity in breast cancer patients was higher than that observed for the overall Spanish population (Fig. 2). The evidence on the association between obesity and cancer can be extended also to increased risk of oesophageal adenocarcinoma, cancers of the pancreas, colorectum, endometrium, and kidney as well as gallbladder and hematological cancers.

Obesity in seniors (>65 years old) is growing as well. In the elderly, obesity contributes to early onset of chronic morbidity and functional impairment. However, addressing the

problem of obesity in seniors is complicated by lack of consensus regarding the potential harms of obesity, the definition of obesity and the need for treatment of obesity in the elderly. Despite the well documented evidence on the links between adverse adiposity and chronic illnesses, little is published on its association with common quality of life symptoms usually attributed to ageing, including impaired physical, psychological and sexual functions.⁷ For this reason the European Male Ageing Study (EMAS) was performed and currently results from this study evidenced that many of the complaints and health problems commonly associated with impaired quality of life in older men are accounted for by increased body fat including those with large waists who are not considered to be "obese" according to BMI.⁷

Taking together, obesity exerts major burdens on health care in many ways, from obesity-related conditions to the hidden costs of personal care and indirect costs associated with absenteeism, disability, premature mortality and workers' compensation. Thus, the health care costs of obesity represent 9.1% of all medical spending in US which reaches 7.5% in Spain.⁴ Therefore, there are an urgent need to investigate those factors associated to the obesity onset and its comorbidities with the objective of characterizing and understanding the molecular mechanisms that lead to this metabolic disorder and finally to design new therapeutic strategies.

Currently, the therapeutic objectives are targeted to counteract the obesity comorbidities and to reduce the impact of the future medical complications related to the excess of body weight. Diverse therapeutic strategies have been assayed to decrease body adiposity. Thus, the improvement of dietary habits together with an increase in the physical activity and behavioral support, are the first line of election treatment to moderately obesity and overweight.⁸ Drug administration and bariatric surgery also can be useful in more extreme cases.⁹ Nutritional interventions, such as caloric restriction diets, can be an efficient therapeutic approach to promote weight loss in obese patients.^{10,11} Although most therapeutic trials involving drugs or dietary treatments show mean weight losses higher than 5% of body weight, the long-term success of maintaining the weight loss is usually poor.^{12,13} In this regards, we have recently demonstrated that after weight reduction induced by an 8-week balanced hypocaloric diet, patients who regained $\geq 10\%$ of the lost weight (regainers) have higher leptin levels and lower ghrelin levels than those who maintained the lost body weight (non-regainers). Interestingly (Fig. 3), this result suggests the existence of two different predetermined populations of patients according to the leptin and ghrelin levels conditioning the weight maintenance outcomes.¹² Therefore, the identification of factors associated with weight regain can enhance our understanding regarding energy homeostasis regulation and would have positive implications in the personalization of therapeutic approaches to obesity.

The prevention of obesity is a key issue in the health policies of any developed country.¹⁴ Health authorities and scientific studies recognize that the health risks associated with obesity are reduced dramatically with weight loss, even without reaching the ideal weight for each individual. Among the measures to be implemented include the labeling

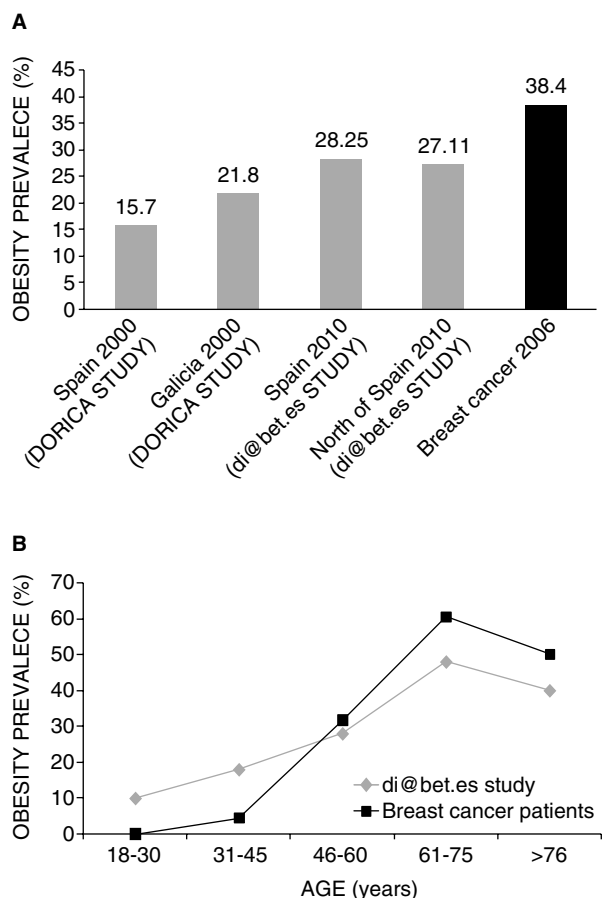


Figure 2 Obesity prevalence between diagnosed breast cancer patients. A) Comparing with obesity prevalence in overall Spanish population and North of Spain estimated in the Spanish population of 25 to 64 years old during 1990-2000 (DORICA study) and the Spanish population older than 18 years old during 2008-2010 (di@betes study). Both studies were based on a pooled analysis of regional cross-sectional random population surveys where the body and height measures were direct data assessed by trained nurses and nutritionists. B) Distribution of obesity prevalence regarding to age range in breast cancer patients and overall Spanish women according to the di@betes study.⁶

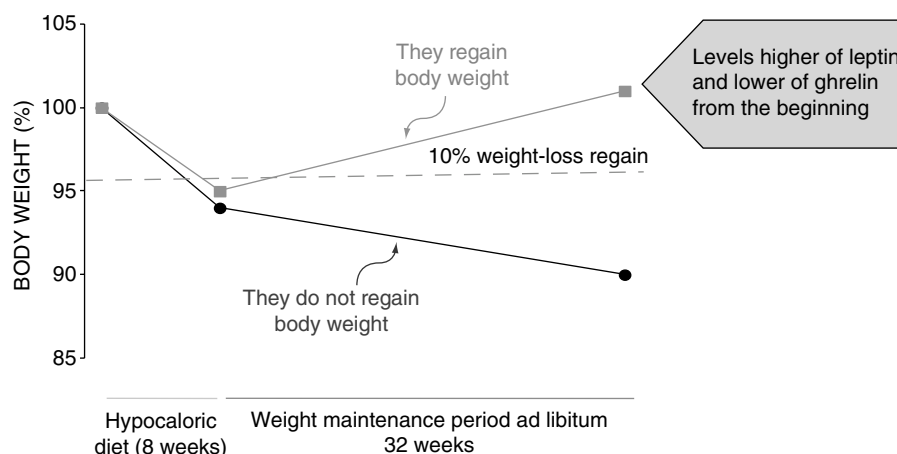


Figure 3 Circulating leptin and ghrelin levels from baseline influence weight regain predisposition after a hypocaloric-diet induced weight loss.¹²

of foods with a more accurate and more information about the properties of food. Measures are needed against the excessive power of marketing on food habits and preferences, protecting especially children.

Another point on which the action is important is the price of food. This is particularly uncomfortable in the sense that for many years has tried to reduce the price of staple foods to improve quality of life and ensure access to food for all economic classes. However, the intervention in prices has also led to the increased cost of products to promote healthy diets such as fruits and vegetables. It is therefore necessary to review the financial structures that control the prices of these foods and indirectly encourage consumption of foods high in fat and calories.

In conclusion, the increasing prevalence of obesity and its upward trend in the overall adult population make this metabolic disturbance a priority risk factor in the implementation of several disease prevention and control strategies. For these reasons, there must be a joint effort of the different governments, scientific community, industries of food, education authorities, legislators and patients and the general population. Importantly, the identification of factors associated with weight gain is a key issue to design personalized therapeutic strategies to obesity. Governments should also restrict the number of unhealthy food establishments such as fast food restaurants. A valid alternative could be the model used to restrict the consumption of alcohol and smoking during the past years.

Conflicts of interest

The authors declare that they have no conflicts of interest in this article.

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