

The Epidemics of Obesity and Cancer

No simple remedy

Moza Al-Kalbani¹ and *Ikram A. Burney²

وبائيات السمنة والسرطان لا يوجد علاج بسيط

موزه الكلبانية وإكرام بيرني

*Thou seest I have more flesh than another man, and therefore more frailty.*¹

OBESITY AND CANCER ARE REGARDED AS two major epidemics of the 21st century.² It has now been well established that obesity is a cause of several cancers, including cancers of the colon, post-menopausal breast, uterus, pancreas, gall bladder, liver, oesophagus and kidney.² It has been estimated that as many as one-third of all cancers can be attributed to an unhealthy diet (such as high caloric intake, high intake of red and processed meat and low intake of fibre) lack of physical activity and obesity. As many as 3% of all the cancers in men and 9% of those in women can be attributed directly to obesity.³ As a result, the World Cancer Research Fund and the American Institute of Cancer Research (WCRF/AICR) have issued guidance on the prevention of cancer in the form of 10 recommendations, one of them being: “be as lean as possible without becoming underweight”³

In this issue of SQUMJ, Moten *et al.* have drawn attention to the very important question as to whether cancer survivors attempt to lose weight.⁴ According to GLOBOCAN, 14.1 million cancer cases were diagnosed in 2012, there were 8.2 million deaths and 32.6 million cancer survivors; all these numbers were shown to be increasing.⁵ A cancer survivor is defined as an individual with a diagnosis of cancer, regardless of the course of illness, until the end of his/her life. Epidemiological evidence suggests that cancer survivors who are obese and overweight are at an increased risk of cancer relapse/progression.³ Hence, after the diagnosis of cancer, survivors maybe interested to learn how they could reduce the chances of cancer progression or relapse.⁶ Clearly, if an exposure is associated with developing cancer and if that exposure continues, then the risk of subsequent cancer progression and/or relapse would be high.⁶ The WCRF/AICR recommend that cancer survivors

follow the recommendations for cancer prevention including maintaining a healthy body weight. The question then arises—is there clear evidence that achieving and maintaining a lean body mass actually leads to a reduction in the incidence of cancer?

Although there is no evidence in the form of phase III studies, epidemiological evidence is strong. Robust data have emerged to suggest that the control of obesity and related lifestyle factors leads to the prevention of cancer. The European Prospective Investigation into Cancer and Nutrition (EPIC) study⁷ and the VITamins And Life-style (VITAL) study⁸ are large prospective studies that have addressed the question. Lifestyle modifications, including a reduction in body weight, actually lead to a reduction in the incidence of and mortality from cancer.^{9,10} More recently, a scientific rationale for this connection has begun to emerge as the biological mechanisms which suggest that obesity is a cause of cancer are beginning to be better understood.¹¹

Fat tissue is now considered to be an endocrine organ, which secretes adipokines, mainly leptin. Leptin induces the upregulation of transcription factors through activation of PI3K, MAPK and STAT3 pathways. Pro-inflammatory cytokines, such as TNF- α , IL-2 and IL-10 (secreted by the adipose tissue) lead to the activation of transcription factor NF- κ B. Adipose tissue also produces steroid hormones, such as oestrogens, progesterone and androgens; these are pro-inflammatory and lead to the activation of various transcription factors. Importantly, insulin and insulin-like growth factor 1 (IGF-1) which are elevated in people with obesity, signal through the Akt/PI3K/mTOR pathway, which in turn leads to the release of leptin and inflammatory cytokines [Figure 1].¹¹

As a result of the combined secretion of adipokines,

¹Department of Obstetrics & Gynaecology, Sultan Qaboos University Hospital; ²Department of Medicine, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Oman

*Corresponding Author e-mail: ikramburney@hotmail.com

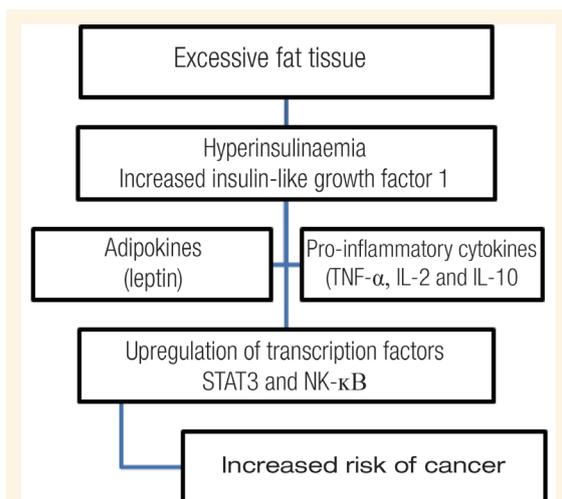


Figure 1: Biological explanation of increased risk of cancer amongst obese patients.

pro-inflammatory cytokines, steroid hormones, a state of persistent hyperinsulinemia, and the resultant continuous upregulation of transcription factors, the risk of cancer progression or its recurrence are higher amongst obese cancer survivors. Furthermore, cancer survivors have an increased risk of morbidity and mortality, not only from cancer, but also from competing factors, such as heart disease, and psychological disturbances [Figure 2].¹¹

Not only is the risk of recurrence and the morbidity and mortality higher among obese patients, but obesity also poses significant challenges in cases where subsequent treatment is needed. The challenges are present right through the stages of diagnosis and surgical and medical management, and even when trying to maintain good pain control. One of the surgeon's nightmares is to operate on an obese patient. Based on the concept that the aim of cancer surgery is to perform a radical excision, the accessibility of organs and the technicality of procedures for an obese patient present a major challenge for the course of the surgery. Specific procedures like pelvic and para-aortic lymph node dissection are sometimes omitted which compromise the process of optimal treatment. Post-operative complications such as ulnar neuropathy, deep vein thrombosis, right ventricular failure, atrial dysrhythmia and aspiration pneumonia are more frequent in obese patients.^{12,13} Obese patients also present challenges to the anaesthesiologist while the pharmacokinetics of most drugs and the responses to some medications are altered by obesity. Chemotherapy can therefore be under- or over-prescribed for obese patients.

Another question then arises, what can be done to curb obesity and its attendant complications in cancer survivors? The American Society of Clinical Oncology

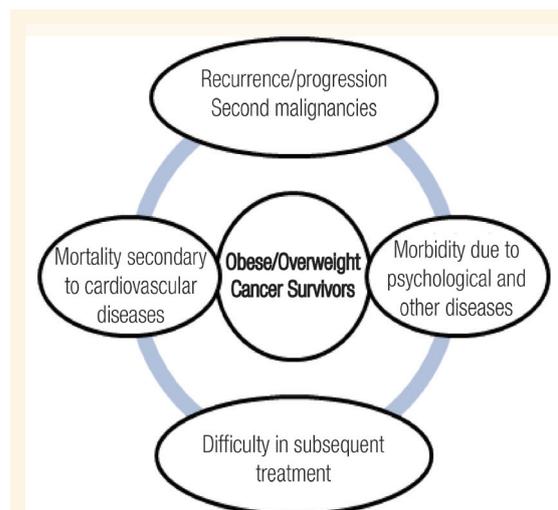


Figure 2: Subsequent risks amongst cancer survivors.

(ASCO) has published guidance for cancer survivors on weight reduction strategies.¹⁴ While the main focus is still on 'lifestyle modifications,' other strategies, such as weight loss drugs and bariatric surgery, are indicated for a selected few; however, the long term consequences of these treatments are not known. Cancer survivors in Moten *et al.*'s study did not demonstrate greater effort to lose weight compared to people with no history of cancer. This was despite having been through the ordeal of the diagnosis of cancer and the subsequent treatment.⁴ Why? Is it because of a lack of awareness and motivation amongst the survivors, or is it because the task is overwhelming and they feel it is too late to remedy the situation? The answer is probably all of the above. The authors of this editorial believe that just conducting a 'fire-fighting campaign' to treat obesity *after* the diagnosis of cancer may not be effective. The seeds of obesity are laid in childhood, or even before, and that is why obesity is turning into one of the epidemics of the 21st century.¹⁵ For example, it has been suggested that environmental influences during physical development increase the susceptibility to both obesity and cancer in adulthood by reprogramming of the epigenome.¹⁶ This is perhaps one of the many reasons that up to one-third of the children in developed countries such as the USA, and one-fifth of those in developing countries, like Oman are obese—and the incidence is on the rise.¹⁷

This epidemic is assuming alarming proportions, especially since obesity can cause cancer in the first place, as well as increasing the risk of subsequent cancers in survivors. There is no simple remedy. Serious efforts are required to modify not just individual lifestyles, but the overall environment to make it easier for individuals to make healthy choices in terms of food and physical activity. The provision of

healthy food in schools, offices and eating places, the availability of walking and cycling tracks and facilities for regular exercise, in addition to time allocation for physical activities during school and work, are only a few suggestions which can create an environment conducive to a healthy lifestyle and curb the dual menace of obesity and cancer. Everybody should play a part—parents, curriculum designers, the media, the food industry, members of civil society, politicians and policy makers.

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