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## International panorama

## Metabolic surgery and cancer

## Cirurgia metabólica e câncer

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Ashrafian H et al. published in the prestigious journal *CANCER*, in May 2011, an extensive review on the beneficial effects of bariatric surgery over the decrease of cancer cases in obese people who underwent this surgery.<sup>1</sup>

Bariatric surgery causes several anatomical and physiological alterations, such as bile flow, decrease of stomach size, change of nutrients flow in the intestine, and modulation of intestinal hormones.

The clinical treatment for obesity has been discouraging since it is not able to maintain weight loss in the long term. The use of metabolic surgery accounted for 350 thousand patients operated worldwide up to that date. In these patients weight decreased sustainably and there was a beneficial effect over the so-called metabolic syndrome. One unexpected result in these operated patients was the declining rates of cancer versus non-operated obese patients.

The surgery leads to a decrease in caloric intake, which on its own decreases carcinogenesis, as demonstrated by several studies. Other factors also influencing the decrease in cancer rate are increased physical activity allowed by weight decrease, and changes in insulin levels, hormonal factors and inflammatory mediators.

Obesity is associated with chronic inflammation caused by the increase of interleukins and tumor necrosis factor. These inflammatory mediators eventually become carcinogenic. With weight loss, there is a change in these factors ultimately leading to the decrease in inflammation and carcinogenesis. Six months after the metabolic surgery, interleukins decrease,

leading to a higher activity of natural killer (NK) cells, and thus resulting in an increase of antitumor immune response.

Another important factor in reducing cancer rates is the decrease of hepatic steatosis in patients who underwent metabolic surgery. The decrease of steatosis leads to the decrease of hepatic inflammation and consequent decrease of cirrhosis and liver cancer. The decrease in leptin production by fat cells in operated patients also leads to a decrease in tumor rate, since leptin is a stimulant of carcinogenesis. Changes in concentrations of sex hormones also leads to the reduction of breast cancer, for instance, in women who underwent metabolic surgery.

Intestinal hormones such as ghrelin (which reduces after metabolic surgery) is also carcinogenic, especially regarding neuroendocrine tumors, gastrointestinal tumors, and prostate cancer.

Metabolic surgery is increasingly performed worldwide due to the advances of the obesity epidemic. Due to its profound metabolic effects, these procedures are no longer considered mere interventions for weight loss, and are increasingly applied in patients with lower body mass indexes. These procedures show a significant reduction in mortality and incidence of cancer. The protective role of metabolic surgery is stronger for tumors related to female obesity, although the anticancer activity of surgery may include weight-dependent or not effects. These include improvement of insulin resistance with attenuation of metabolic syndrome, as well as decreased oxidative stress and inflammation, the beneficial modulation

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of sex steroids, intestine hormones, interleukins decrease and modulation of the immune system. Elucidating the precise mechanism of the metabolic surgery in cancer prevention can increase our understanding of how obesity, diabetes and metabolic syndrome are associated to oncogenesis.

This will require controlled and randomized *in vitro* and *in vivo* (animal models) carcinogenesis studies and metabolic surgery, which can result in the refinement of metabolic operations to maximize their anticancer effects. This can also offer new treatment approaches for tumors.

Bariatric surgery started with the sole aim of decreasing the weight of morbidly obese patients, but it has accidently widened the unexpected or initially planned benefits from surgery. In addition to the already established changes in

quality of life and reduction of comorbidities, such as diabetes and hypertension, now rates of cancer in patients who underwent bariatric and metabolic surgery have decreased compared with non-operated obese patients.

This opens a wide field of medical research, and certainly the benefits of this treatment will bring new and good surprises in the future!

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R E F E R E N C E

1. Ashrafian H, Ahmed K, Rowland SP, Patel VM, Gooderham NJ, Holmes E, et al. Metabolic Surgery and Cancer. *Cancer*. 2011; 117:1788-99.