

The catastrophic effect of obesity on blood vessels

Richard Béliveau

Translated from Le Journal de Montréal, December 19th, 2022

A systematic analysis reveals that excess weight has several negative effects on the function of so-called endothelial cells that line the blood vessels of different organs.

The World Health Organization recently reported that there are currently one billion people in the world who are obese, including 340 million teenagers and 40 million children (1).

The immediate consequence of this high prevalence of overweight is to dramatically increase the risk of developing a very large number of chronic diseases and thereby to amputate several years of life expectancy for these overweight people (2).

Several factors contribute to the sharp increase in disease risk observed in overweight people.

For example, excess fat is known to disrupt metabolism (the insulin response, in particular) and create pro-inflammatory conditions conducive to the development of certain diseases, including type 2 diabetes and certain types of cancer.

It also seems that the increase in pathologies associated with overweight is due to a direct negative effect of excess fat on several organs.

In this sense, it is remarkable that diseases as diverse as atherosclerosis, heart failure, neurodegeneration, stroke, pulmonary hypertension, renal vascular disease and hepatic vascular complications are all caused, at least in part, by dysfunction of blood vessels.

It is therefore possible that the blood vessels are particularly vulnerable to the upheavals caused by overweight and contribute to the development of pathologies affecting several distinct organs.

INDIVIDUAL VARIATIONS

To assess this possibility, a team of German researchers used modern transcriptomic techniques to measure the RNA concentration of thousands of genes in endothelial cells present in different organs from obese animals (3).

Since these endothelial cells line the inside of blood vessels, they are in close contact with the bloodstream and therefore directly exposed to changes caused by excess fat.

Systematic analysis of 375,000 distinct endothelial cells from seven different organs (brain, lung, heart, kidney, liver, visceral adipose tissue and subcutaneous adipose tissue) revealed that obesity caused significant disturbances in the expression of several genes by these cells.

However, these changes are very different from one organ to another: for example, the genetic variations observed in the liver mainly affect lipid metabolism, while the kidney vessels are much more sensitive and develop serious metabolic dysfunctions.



Endothelial cells in the lung, on the other hand, have a large excess of inflammatory molecules, which could contribute to the increased susceptibility of obese people to respiratory viruses, as has been observed during the COVID-19 pandemic, with obesity as a major cause of hospitalization and death among adults under 50 years of age.

The cells of the vessels of the brain, for their part, show a decrease in the genes involved in the transport of molecules from the blood to the brain (which would contribute to the demonstrated link between obesity and neurodegeneration).

The cells of the vessels of the heart show an increase in genes involved in the development of atherosclerotic plaques, in agreement with studies showing that obesity accelerates the process of atherosclerosis and represents an important risk factor for cardiovascular accidents.

An interesting aspect of the study is to show that these variations are largely reversible by modifications to the diet of the animals in order to avoid excess weight.

Here again, surprisingly, the response of the vessels depends on their anatomical location: the endothelial cells of the liver recover completely after having eliminated the obesogenic diet, those located at the level of the heart only partially return to their normal state while those of the kidney do not show any progress.

These results suggest that the function of most blood vessels can be improved by adopting better dietary habits, but that damage may remain in certain organs. Another argument in favor of an aggressive approach to prevent the development of obesity as much as possible, especially in children and teenagers, to avoid prolonged exposure of vital organs to the harmful effect of excess fat.

The prevention of overweight should be an individual and societal priority in our overall vision of health, like the prevention of smoking.

- (1) ONU Info (March 4th, 2022). Plus d'un milliard de personnes dans le monde sont obèses (OMS). news.un.org/fr/story/2022/03/1115672.
- (2) Prospective studies collaboration. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet* 2009; 373: 1083-1096.
- (3) Bondareva O et al. Single-cell profiling of vascular endothelial cells reveals progressive organ-specific vulnerabilities during obesity. *Nat. Metab.* 2022; 4: 1591-1610.