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EDITORIAL

ABDOMINAL OBESITY: THE TIP OF THE CARDIOMETABOLIC RISK ICEBERG!

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This issue of the **CMRe**Journal features 3 brief review papers that report on the key notions discussed during a symposium of the International Chair on Cardiometabolic Risk held in January 2009 at the XIXes Journées Européennes de la Société Française de Cardiologie annual meeting. In the first article, Dr. Paul Poirier describes how to identify the patients who have "at-risk" obesity and how to manage these patients in order to reduce the risk of future cardiovascular events. He also discusses the apparent "obesity paradox". The second short review, written by Dr. Éric Larose, deals with the patients who are at a more advanced stage of their "cardiometabolic disease", i.e., those who have developed coronary heart disease (CHD) and require percutaneous coronary intervention. The review article by Dr. Patrick Mathieu presents the important and multifaceted implications of cardiometabolic risk in the context of cardiac surgery. These brief, insightful reviews are followed by a "Special Article" written by Dr. Michael Jensen from the Mayo Clinic (Rochester, MN) that deals with what has been referred to as "normal weight obesity". Dr. Jensen makes the key point that assessment and management of patients should focus on their health, not only on their body mass index or percent body fat. Finally, we are grateful to another member of the Chair, Dr. Luis M. Ruilope from Hospital Octubre (Madrid, Spain), who generously wrote an "Original Article" on ambulatory pressure, which adds relevant information to the assessment/management of obese hypertensive patients.

Intra-abdominal (Visceral) Obesity: the "At-Risk" Obesity

Obese individuals are not all at equal risk of developing metabolic and life-threatening complications. There is a strong body of evidence supporting the concept that fat distribution and deposition in non-adipose tissues (liver, heart, muscle, pancreas) instead of subcutaneous adipose tissues is an important determinant of this inter-individual difference in the risk associated with obesity [1-3]. In the quest to identify the patients with "at-risk" obesity, several definitions and parameters have been proposed [4]: 1) Obesity defined as a body mass index $\geq$30 kg/m^2. This index is a crude marker of excess fat but does not account for the inter-individual variability in body fat distribution; 2) Ab-

dominal obesity, which refers to an increased waist circumference. The addition of this easily measurable parameter is an important step in the identification of "at-risk" obesity. However, the main limitation of this parameter is that it does not differentiate between intra- (i.e., visceral) vs. extra- (i.e., subcutaneous) abdominal fat; 3) Intra-abdominal obesity, which can be identified and quantified using imaging techniques such as computed tomography or magnetic resonance imaging and/or by the combination of increased waist circumference and specific blood metabolic abnormalities such as hypertriglyceridemia (hypertriglyceridemic waist). More recently, the term "ectopic fat" has been used in addition to intra-abdominal obesity. This term is more accurate than the latter in the sense that it refers to fat accumulation in non-adipose tissues, including viscera and muscles. Furthermore, it crystallizes the point that excess energy should normally be stored in the subcutaneous compartment and that this subcutaneous fat is rather protective. To this effect, it is important to remember that without this reserve of subcutaneous fat, human beings would probably have disappeared a long time ago. The excessive deposition of fat outside of the subcutaneous compartment is abnormal and leads to a cascade of metabolic and cardiovascular complications. Hence, subcutaneous fat constitutes a caloric reserve that may eventually be life-saving in some circumstances, whereas ectopic fat is associated with a dysmetabolism that may considerably shorten life expectancy.

The Multiple Target Organs of Intra-abdominal Obesity

Beyond the contribution of mere obesity, the crucial importance of pathophysiological processes associated with intra-abdominal adiposity/ectopic fat to the development of type 2 diabetes, atherosclerosis, and cardiovascular disease has been recognized in numerous studies and recently referred to as "cardiometabolic risk" [1-3] (Figure). Initially, most of the studies have focused on the link between abdominal or intra-abdominal obesity and the risk of CHD or stroke. When analyzed collectively, these studies suggest that the cluster of metabolic abnormalities linked to intra-abdominal obesity is associated with a 2-fold increase in the relative risk of CHD/stroke events [5]. However, the deeper the scientists dig on intra-abdominal obesity, the more metabolic abnormalities and target organs are identified (Figure). Recently, intra-abdominal obesity and associated dysmetabolism have been linked to increased risk of: 1) aortic valve disease; 2) degeneration of bioprosthetic heart valves; 3) operative mortality and atrial fibrillation following coronary artery bypass surgery; 4) adverse left ventricular remodelling and heart failure; 5) renal dysfunction; 6) sleep apnea; 7) cancer; 8) aging-related cognitive decline, etc. In summary, intra-abdominal adiposity/ectopic fat is associated with a cluster of diabetogenic and atherogenic abnormalities that, in turn, negatively affect several target organs including liver, heart, brain, kidneys, muscles, etc. (Figure). Ectopic fat deposition may also act directly on the target organs through the lipotoxicity phenomenon and/or the release of locally acting molecules. Another worrying aspect of intra-abdominal obesity is that this phenotype is not exclusively limited to the adult and elderly populations. It is also now frequently encountered in children and teenagers and is associated with early alterations of their metabolic profile. Hence, in coming decades, our healthcare system will have to face up to the catastrophic consequences of these millions of time-delayed, metabolic bombs.

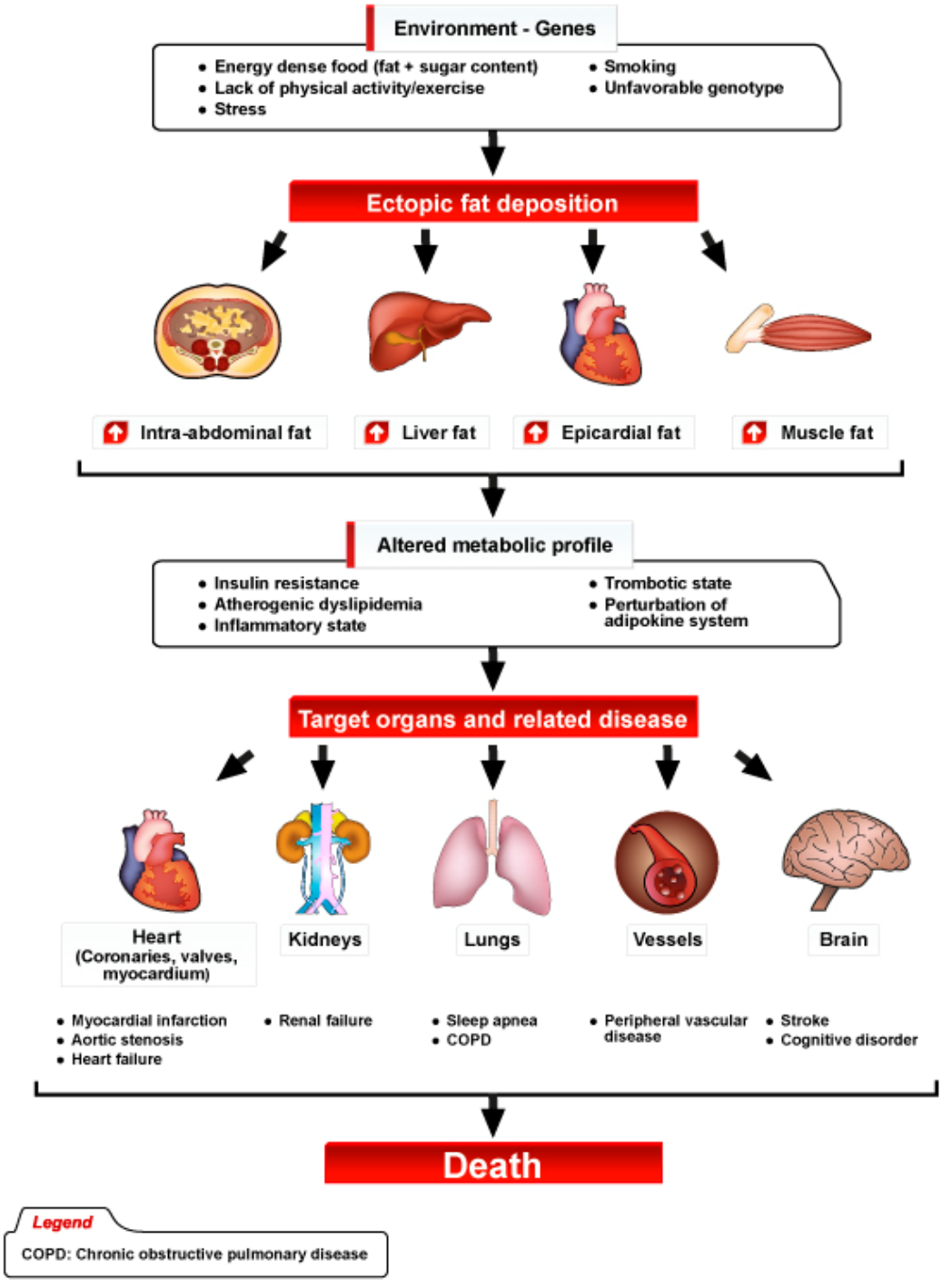

Figure: Determinants and consequences of intra-abdominal adiposity/ectopic fat.

Unanswered Questions

There are several unanswered questions that will need to be addressed in future studies:

1) What are the determinants of intra-abdominal adiposity/ectopic fat? Why, for the same positive energy balance, do some patients develop subcutaneous obesity with no or little alteration of their metabolic profile, whereas others develop the intra-abdominal obesity generally accompanied by an increased cardiometabolic risk?

2) Why do some (a few) patients with excessive intra-abdominal adiposity/ectopic fat accumulation nonetheless exhibit a normal metabolic profile? Are they genetically lucky individuals?

3) Is intra-abdominal adiposity/ectopic fat a factor actively contributing to the development of metabolic and life-threatening complications ***OR*** is it just a risk marker?

4) If we target and reduce intra-abdominal adiposity with the use of behavioural or pharmacological interventions, does this translate into significant reduction of metabolic and life-threatening complications? The presentation of such data would certainly help us to clarify the exact pathophysiological role of intra-abdominal adiposity/ectopic fat: i.e., is it a ***risk marker or a risk factor?***

Implications for Clinical Practice

Pending further studies to answer these important questions, it is urgent to implement strategies at the different levels of clinical practice to systematically identify the patients who have "at-risk" obesity, i.e., intra-abdominal adiposity/ectopic fat. This at-risk phenotype remains largely undiagnosed and untreated in current practice. One approach to detect and quantify ectopic fat would be to use computed tomography or magnetic resonance imaging, but this approach is expensive and does not apply to routine screening in general practice. As it is often the case in medicine, the simpler, the better, and in this regard waist circumference is a simple and cost-effective measure to identify abdominal obesity. The IDEA study provided convincing evidence that this measurement can successfully be used in general practice and that it provides important information for the patient's prognostication [6]. Hence, waist circumference should be systematically measured as part of the routine physical exam. The second step is to combine the measurement of waist circumference with the measurement of triglycerides to further track down the intra-abdominal (i.e., visceral) obesity phenotype. The hypertriglyceridemic waist phenotype is the clinical tool that likely offers the best compromise between accuracy, simplicity, and cost-effectiveness to identify "at-risk" obesity [7]. The algorithms of the National Cholesterol Education Program-Adult Treatment Panel III or the International Diabetes Federation can also be used but are more complex and require the measurement of more parameters [8].

Individuals with Intra-abdominal Adiposity/Ectopic Fat: Next Steps

The first line of treatment should logically focus on aggressive lifestyle changes, including improving eating habits and encouraging patients to be more active on a daily basis. In this regard, we clearly need more data on the applicability and long-term efficacy of lifestyle modification programs

in intra-abdominally obese individuals. Moreover, we can anticipate that a significant proportion of patients with intra-abdominal obesity will not respond to lifestyle modification programs and that pharmacological intervention may be required in these patients. However, to date, the pharmacotherapy targeting intra-abdominal obesity remains very limited and has significant side effects. More research and development are thus urgently needed to fill this gap in the arsenal that clinicians need to efficiently fight intra-abdominal obesity.

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