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EDITORIAL

Cardiovascular risk, Metabolic disease and NASH control for Health Empowerment: Future endeavours☆

Control del riesgo cardiovascular, la enfermedad metabólica y la esteatosis hepática a través del empoderamiento de la salud: una propuesta de futuro

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In spite of the advances in the knowledge about the metabolic diseases that negatively impact systemic vascularisation, there are still gaps in the area of vascular risk, as can be seen from the evolution in clinical guidelines and the lack of explanation for at least 10% of the vascular diseases.[1] The discovery of new expressions of metabolic diseases, such as non-alcoholic steatohepatitis, is of interest in establishing a complete definition from the viewpoint of cardiovascular risk. Studies such as that of Elosua-Bayes[2] show that the disease from fatty infiltration of the liver increases our understanding og metabolic deregulation and vascular disease. This association also seems to provide a ''plus'' to the knowledge in the area, demonstrating that a capacity to predict cardiovascular events and mortality might exist, independently of the rest of consolidated risk factors.[3] However, it is difficult to make a clinical interpretation without considering the three vertexes of the triangle formed by non-alcoholic steatohepatitis, metabolic disease and vascular disease.

From the cardiometabolic point of view, the relationship between obesity, non-alcoholic steatohepatitis and cardiovascular risk is mainly marked by three factors: Lipid accumulation,[4] insulin resistance[5] and oxidative stress.[6] The last one is the trigger of what is known as the ''second hit'': the inflammatory potential to set off the progression to the more serious forms of hepatic disease.[7] Although scientific advances are gradually untangling the importance of the genetic component in this trio,[8] there is undoubtedly a relationship between lifestyle (understood, in a simplified manner, as diet, exercise and sleep) and the hepatic disease due to fat accummulation.[9,10] Nevertheless, there are two barriers that keep the disease of liver fat accumulation from being considered a ''translational'' entity, including the difficulty in diagnosis and treatment. So much so that the current recommendations from the American Association for the Study of Liver Diseases (AASLD) clarify screening of this disease because of the absence of accurate diagnostic methods and lack of effective treatment.[11]

On the one hand, diagnostic methods continue to depend conceptually on the hepatic biopsy as the gold standard, which associates a mortality that is hard for the patient to accept outside of the context of clinical trials. However, indirect methods of diagnosis (both structural with

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technology of attenuation of controlled parameters,[12] and biochemical with diagnostic scales such as the ''fatty liver index — FLI,''[13] among others) are reaching sensitivity and specificity benchmarks that are sufficient for elimination of the hepatic disease. In addition, any potential deficits in distinguishing should be evaluated within the slow history of this disease from liver fat deposits and remembering the fact that this condition overlaps with other metabolic disorders, both in diagnosis and in treatment. In this regard, the research into new calculations or ''scores'' such as HSI, BAT, FIB4, etc., along with metabolomics advances, represents viable, consistent and problem-solving alternatives in the diagnostic sphere.

On the other hand, interpretation of cardiovascular risk is gradually becoming more integrated. The latest guidelines on preventing lipid accumulation are based on individual risk to set cholesterol levels.[14] This interpretation of risk encourages using all the resources available in assessing patients as a preliminary step for deciding on the lipid control to be achieved. Continuing with this tendency, it seems possible to include non-alcoholic steatohepatitis in the clinical sphere of short-term cardiovascular diagnosis. This would also include the implications from the point of view of diagnostic effort.

Drug therapy is another barrier in the transition from research to clinical practice. Treatment with antioxidants seems to have a moderate effect on the progression of hepatic disease.[15] The truth is that its recommendation is in doubt because of the characteristics of its clinical trials and its potential toxicity at high doses.[11] There are also drugs for diabetes control (such as pioglitazone) that have shown a quantitative improvement in the state of hepatic fat infiltration. However, they have not proven a direct activity on steatosis; neither do they seem appropriate for treating patients not having this disease, taking the potential increase in cardiovascular risk associated with this drug into consideration.[11] With that in mind, the analogues of GLP-1 are promising, especially after they have received approval as a treatment for obesity in non-diabetic patients.[16] Well-designed clinical studies are nonetheless needed, ones that make it possible to distinguish between how much of the effect is due to weight loss and how much is related to the direct effect of these analogues on hepatic fat.

This framework of diagnostic-therapeutic uncertainty seems to diminish the importance of one of the core causes of the evolution of these diseases: lifestyle. These days, lifestyle interventions still present several difficulties in everyday clinical practice, such as the lack of time, the absence of specific training, the appearance of competitive models that lie outside the medical sphere, and the lack of adherence to the general advice. In spite of these factors, specific intervention maintained over time on lifestyle habits (diet, exercise, sleep and psychological state) has demonstrated an important effect, both on obesity and on its consequences,[17] with hepatic steatosis among them.[18] In addition, the most spectacular results have been in populations that took on the changes through their own decisions.[19] A healthy lifestyle also presents an obviously lower ratio of secondary effects in comparison to drug intervention, while such a lifestyle has an effect on the patients' perception of quality of life, too.[20]

In short, although non-alcoholic steatohepatitis is related to vascular and metabolic diseases, the clinical approach to this entity requires greater research in the therapeutic and diagnostic levels. Changing the clinical focus in the assessment of and intervention on life habits might also have an interesting positive impact on this disease. This effect would be come about through the interactions among lifestyle modifications, drug support and health empowerment from the patient, with results at the levels of preventing the disease and improving quality of life as well. From a practical point of view, recent findings seem to favour the gradual inclusion of specialists in non-alcoholic steatohepatitis in multidisciplinary cardiovascular risk prevention units. Lifestyle research should also be backed by the training of physicians specialised in this area. In this context, consultation on patient lifestyle could be perfect for achieving the following results:

Uniting the different profiles of vascular and metabolic patients; (ii) diagnosing deviations from a healthy lifestyle; (iii) implementing measures in the area of lifestyles with the backing of specialists in dietetics, physical activity, rehabilitation and sleep; (iv) introducing the assessment of the impact of habits on quality of life in clinical terms; and (v) training the patients individually as to healthy habits in order to favour wellbeing and health empowerment for each person.

In conclusion, the fact that metabolic risk in its varied manifestations (non-alcoholic steatohepatitis, obesity and vascular risk) is so important justifies the research and training in the area and the efforts to implement them in a way that is translational, unitary and consistent in normal clinical practice.

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