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Fatty liver and diabetes:

new strategies for screening, risk assessment, and treatment of metabolic liver disease in people with type 2 diabetes

Metabolic dysfunction-associated steatotic liver disease (MASLD) has become one of the most common complications of type 2 diabetes mellitus (T2DM). The close relationship among insulin resistance, obesity, and hepatic fat accumulation makes MASLD another manifestation of the cardiometabolic continuum affecting many people with diabetes.1,2 Important advances have occurred in recent years. The new international nomenclature has been widely adopted, leading scientific societies recommend systematic screening in people with T2DM, and new therapeutic evidence is changing the clinical management of this disease.3,4,5 Furthermore, from the perspective of family medicine, the recently proposed diagnostic and therapeutic algorithm from the Fundación redGDPS provides a practical tool for incorporating MASLD management into routine primary care.6,7 This article reviews the most relevant changes and their implications for people with diabetes.

MASLD: MUCH MORE THAN A CHANGE OF NAME

One of the most visible changes in recent years has been the replacement of the term NAFLD *(nonalcoholic fatty liver disease)* with MASLD. Although this may seem merely terminological, it represents an important conceptual shift. The new name places metabolic dysfunction at the center of the disease and avoids defining it exclusively by the absence of alcohol consumption. The new classification recognizes that most people with hepatic steatosis have obesity, diabetes, hypertension, or lipid abnormalities, factors that influence both liver disease progression and cardiovascular risk. Consequently, MASLD should now be understood as a systemic disease rather than solely a liver disease (1, 2).

One point that causes confusion, especially among patients, should be clarified: the change in name does not mean that alcohol is no longer relevant. The new classification includes an intermediate category, termed MetALD, for people with metabolic dysfunction who also consume a significant amount of alcohol. In these individuals, both factors contribute to the disease, and advice about alcohol consumption remains an essential part of treatment.

As a consequence of all the above, MASLD should now be understood as a systemic disease rather than solely a liver disease.

T2DM: THE MAIN SETTING FOR MASLD

The association between T2DM and MASLD is probably one of the strongest in metabolic medicine. The most recent studies estimate that approximately two out of every three people with T2DM have some degree of hepatic steatosis. However, a substantial proportion remain undiagnosed. This is particularly relevant because diabetes accelerates the progression of liver disease. People with T2DM are at greater risk of developing advanced fibrosis, cirrhosis, and hepatocellular carcinoma. Furthermore, several studies have shown that the coexistence of T2DM and MASLD significantly increases the risk of cardiovascular events, the leading cause of death in these patients. Thus, identifying MASLD in a person with diabetes means not only detecting a liver abnormality but also recognizing a marker of increased cardiometabolic risk (8, 9).

THE MAJOR CHANGE: WE ARE NO LONGER LOOKING ONLY FOR STEATOSIS; WE ARE LOOKING FOR FIBROSIS

Perhaps the main development compared with a few years ago is that the purpose of screening is no longer to detect hepatic fat. Most people with T2DM have some degree of steatosis. However, the true prognostic determinant is liver fibrosis. Advanced fibrosis is associated with a significantly increased risk of cirrhosis, liver failure, hepatocellular carcinoma, and all-cause mortality. For this reason, current recommendations prioritize early identification of fibrosis using readily accessible noninvasive tools (8, 9, 10).

One message deserves emphasis because it remains a cause of underdiagnosis: normal transaminase levels do not rule out the disease. Many people with MASLD, including those with advanced fibrosis, have AST and ALT levels within the reference range. Relying on conventional liver blood tests for screening misses a substantial proportion of patients at greatest risk (6).

THE REDGDPS ALGORITHM: A TOOL FOR EVERYDAY PRACTICE

The proposal developed by the Steatosis Group of the Fundación redGDPS is probably one of the most useful contributions to primary care in our setting. The algorithm establishes a simple, stepwise process for selecting people at greatest risk of advanced liver disease (6, 7). In an initial phase, steatosis can be confirmed by ultrasonography or by validated indices such as the Fatty Liver Index (FLI), calculated using body mass index, waist circumference, triglycerides, and GGT: a value < 30 makes steatosis unlikely, whereas values of > 60 suggest a high probability of steatosis. Once steatosis has been identified, the next step is to calculate the FIB-4 (Fibrosis-4) index, which uses age, AST and ALT levels, and platelet count—parameters generally available in »

THE MAIN CURRENT OBJECTIVE OF SCREENING IS NOT TO DETECT HEPATIC FAT, BUT TO IDENTIFY FIBROSIS EARLY

» routine blood tests and electronic medical records (5).

Interpretation is particularly straightforward:

- FIB-4 < 1.3: low risk of advanced fibrosis.
- FIB-4 between 1.3 and 2.67: intermediate risk.
- FIB-4 > 2.67 : high risk of advanced fibrosis.

People with low values may remain under follow-up in primary care, whereas intermediate values require second-line testing, preferably liver elastography. Patients at high risk should be evaluated by Hepatology or Gastroenterology.

This approach makes it possible to rationalize referrals and focus specialized resources on those most likely to benefit.

MOST PEOPLE WITH T2DM AND MASLD REMAIN UNDIAGNOSED DESPITE HAVING AN INCREASED CARDIOVASCULAR RISK

THE ADA ALSO ENDORSES SYSTEMATIC SCREENING

Another important change is the publication of the American Diabetes Association (ADA) consensus report on MASLD in people with diabetes. This document definitively places metabolic liver disease within routine diabetes management and recommends systematic assessment of fibrosis risk in people with T2DM. This message is particularly relevant to primary care: screening for MASLD is gradually changing from an optional activity to another component of comprehensive cardiometabolic risk assessment (3).

NEW THERAPEUTIC OPTIONS

For years, MASLD treatment was practically limited to weight loss and physical exercise. Although these measures remain the fundamental basis of treatment, new alternatives are now available that are changing the therapeutic landscape (11).

- **GLP-1 receptor agonists**

  GLP-1 receptor agonists have demonstrated benefits extending far beyond glycemic control. Weight reduction, improved insulin resistance, and favorable cardiovascular effects are accompanied by a significant reduction in liver fat. Results obtained with semaglutide have shown high rates of resolution of liver inflammation, consolidating its role in people with T2DM, obesity, and MASLD (12)

- **Tirzepatide**

  The emergence of tirzepatide probably represents one of the most important developments in recent years. Available studies show very substantial reductions in body weight, overall metabolic improvement, and a significant reduction in liver inflammatory activity. The results of the SYNERGY-NASH study have reinforced interest in this molecule as one of the most promising strategies for treating MASH.13

- **SGLT2 inhibitors**

  SGLT2 inhibitors continue to occupy a prominent position in the treatment of T2DM. Although they have no specific indication for MASLD, various studies suggest favorable effects on hepatic steatosis, and they retain unquestionable cardiovascular and renal benefits (14).

- **Resmetirom**

  The first specific treatment. The approval of resmetirom represents a historic milestone. For the first time, a treatment has been specifically authorized for MASH with significant fibrosis. Clinical trial results have demonstrated histologic improvement and reduced hepatic inflammatory activity, opening a new era in the management of this disease (15).

WHAT CAN WE DO IN CLINICAL PRACTICE?

People with T2DM should be considered a high-risk population for MASLD. Systematic use of FIB-4 makes it possible to rapidly identify those more likely to have advanced fibrosis. At the same time, therapeutic strategies targeting weight loss, physical activity, and appropriate use of drugs with cardiometabolic benefits can favorably modify disease progression. Integrating the redGDPS algorithm into clinical practice may facilitate earlier detection and more efficient care. **D**

CONCLUSIONS

- MASLD affects approximately two out of every three people with T2DM and remains clearly under-diagnosed.
- Liver fibrosis is the main prognostic marker and should be the primary target of screening.
- The Fundación redGDPS algorithm allows straightforward and effective risk stratification in primary care.
- GLP-1 agonists, tirzepatide, and resmetirom are changing therapeutic management of the disease.
- Early detection of MASLD should be incorporated into the overall assessment of cardiometabolic risk in diabetes.

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