NAFLD Updates: What the Diabetes Care and Education Specialist Needs to Know

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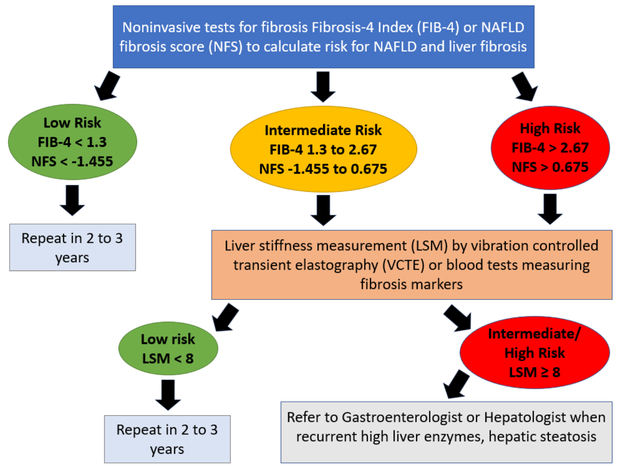
INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is present in over 70% of individuals with type 2 diabetes (T2D), which is twice that in the general population. An individual is said to have NAFLD if on liver biopsy there is evidence of ≥ 5% liver fat with a background history of no alcohol consumption or other liver diseases. NAFLD consists of a spectrum of hepatic disorders that ranges from hepatic steatosis, non-alcoholic steatohepatitis (NASH), advanced fibrosis (AF), cirrhosis, development of hepatocellular carcinoma (HCC), and mortality due to liver disease[1]. T2D and insulin resistance increase NAFLD progression to cirrhosis and increase liver-related all-cause mortality[2,3]. Conversely, NAFLD is associated with a twofold increased risk of developing T2D. In addition, NAFLD is associated with increased cases of both cardiovascular (CV) disease and chronic kidney disease (CKD)[4,5]. Lack of awareness of NAFLD as an emerging complication of T2D remains a challenge among healthcare professionals including Diabetes Care and Education Specialists (DCES). This poster highlights the latest recommendations including assessment, therapeutic management, and monitoring of NAFLD in individuals with T2D.

CLINICAL ASSESSMENT[5,6,7,8,9]

- Screen individuals at high risk for NAFLD, HCC, and advanced fibrosis in the presence of the following markers:
  - T2D or pre-diabetes with cardiometabolic risk factors who have elevated ALT or fatty liver on imaging
  - Obesity or insulin resistance
  - Over 50 years of age
  - Persistently elevated aminotransferases (AST/ALT > 30 units/L) for > 6 months
  - Hepatic steatosis on imaging

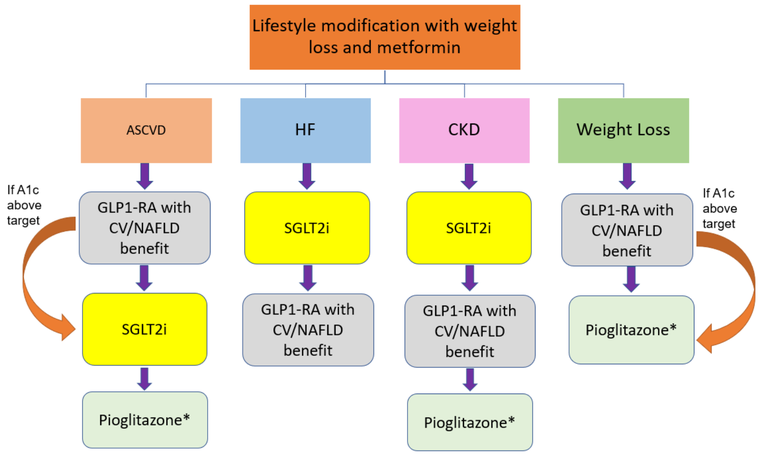
Figure 1: Screening tools and risk stratification



MANAGEMENT[1,6,7,9]

- Lifestyle Modification: Cornerstone of management with a goal of weight loss
  - Weight loss goal of 5%, ideally ≥ 10% improves liver histology
  - Weight loss ≥ 7 to 10% for NASH resolution and improve fibrosis
  - Limit saturated fat, starches, and added sugar
  - Healthier eating patterns such as the Mediterranean diet
  - Aerobic activity and resistance training
- Consider bariatric surgery for individuals with a BMI of ≥ 35 kg/m^2 with NAFLD (caution in compensated cirrhosis patients)
- No medications are approved for treating NAFLD. Medications to treat T2D and NAFLD are selected based on hepatic benefits and weight loss properties
- Pioglitazone (Actos ™): Insulin sensitizer, improves liver fibrosis
- GLP1 receptor agonist (GLP1-RA): Improves hepatic insulin resistance, weight loss, cardiorenal benefits, and improvement in hepatocyte mitochondrial function
  - Liraglutide (Victoza™) treatment resolved NASH, improved hepatic steatosis, reduced progression to liver fibrosis
  - Semaglutide (Ozempic ™): Resolution of NASH without worsening liver fibrosis in individuals with T2D and AF. The 2.4 mg weekly dose reported resolution of steatosis
  - Tirzepatide (Mounjaro™): Weight loss, reduction of ALT & hepatic steatosis. Improved NFS and FIB-4 index
- SGLT2 inhibitors (SGLT2i): Cardiorenal benefits, weight loss, reduction in ALT & magnetic resonance imaging proton density fraction
  - Empagliflozin (Jardiance ™): Improved hepatic steatosis and hepatic fibrosis
  - Dapagliflozin (Farxiga™): Decreased measures of liver stiffness measures on VCTE

Figure 2: Treatment Options for Individuals with NASH and T2D[1,6,7]



ASCVD: Atherosclerotic Cardiovascular Diseases HF: Heart failure
*Pioglitazone: Caution with fluid retention

MONITORING[1,6,7,9]

- Patients with fibrosis at baseline should be monitored at least yearly
- Those without fibrosis: every 2 to 3 years if there is no worsening of metabolic risk factors
- Check AST/ALT and evaluate obesity, hypertension, and dyslipidemia
- Goal is to optimize metabolic parameters in patients with T2D to reduce the risk of ASCVD and CKD
  - Consider goals of A1C < 6.5%, blood pressure < 130/80 mmHg, and LDL < 50 mg/dL
- For those with cirrhosis or high-risk fibrosis progression, refer to a hepatologist for further evaluation and monitoring at least every 6 months
  - May include liver biopsies, varices screening, and HCC surveillance
- Consider enrollment in a clinical trial for NAFLD therapies

CONCLUSION[2,4,5]

There are approximately 18.2 million people in the US with T2D and NAFLD. Over a 20 year period, expected healthcare costs are estimated to be $55.8 billion for these patients with a significant increase in liver transplants, CV-related deaths, and liver-related deaths. Identifying and treating NAFLD early on can prevent the development of more severe liver diseases and deaths. Therefore, it is important for the DCES in primary care and endocrinology practices to have an increased awareness and knowledge about NAFLD. The DCES should encourage people with diabetes to focus on lifestyle modifications with a goal of 5 to 10% weight loss through diet and exercise modifications. While there are no FDA-approved treatments for NAFLD at this time, medications such as pioglitazone, GLP1-RA, and SGLT2i can help with weight management, insulin resistance, and the progression of NAFLD. Further research is needed in this area, but the DCES can work to bring awareness about NAFLD to people with diabetes, colleagues, and other members of the healthcare team.

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