Addendum

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Addendum. 4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2023*. Diabetes Care 2023;46(Suppl. 1):S49–S67

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Section 4, "Comprehensive Medical Evaluation and Assessment of Comorbidities," of the *Standards of Care in Diabetes—2023* has been updated to reflect the current clinical knowledge and evidence in nonalcoholic fatty liver disease (NAFLD).

The online version of the article (https://doi.org/10.2337/dc23-S004) reflects the changes described below.

Zobair Younossi, of Inova Fairfax Medical Campus, Inova Health System, Falls Church, VA, has been added as an author due to his expertise in NAFLD. The author list and disclosures table (p. S281) have been updated accordingly.

Recommendation 4.10 has been replaced by new Recommendations 4.11a, 4.11b, 4.12, and 4.13:

> "**4.11a** Adults with type 2 diabetes or prediabetes, particularly those with obesity or cardiometabolic risk factors/established cardiovascular disease, should be screened/risk stratified for nonalcoholic fatty liver disease with clinically significant fibrosis (defined as moderate fibrosis to cirrhosis) using a calculated fibrosis-4 index (derived from age, ALT, AST, and platelets [https://www.mdcalc.com/calc/2200/fibrosis-4-fib-4-index-liver-fibrosis]), even if they have normal liver enzymes. **B**
>
> **4.11b** Adults with diabetes or prediabetes with persistently elevated plasma aminotransferase levels for >6 months and low fibrosis-4 index should be evaluated for other causes of liver disease. **B**
>
> **4.12** Adults with type 2 diabetes or prediabetes with an indeterminate or high fibrosis-4 index should have additional risk stratification by liver stiffness measurement with transient elastography, or the blood biomarker enhanced liver fibrosis. **B**
>
> **4.13** Adults with type 2 diabetes or prediabetes with indeterminate results or at high risk for significant liver fibrosis (i.e., by fibrosis-4 index, liver stiffness measurement, or enhanced liver fibrosis) should be referred to a gastroenterologist or hepatologist for further workup. Multidisciplinary care is recommended for long-term management. **B**"

New Recommendations 4.14–4.19b have been added:

> "**4.14** Adults with type 2 diabetes or prediabetes particularly with overweight or obesity with nonalcoholic fatty liver disease should be recommended lifestyle changes that promote weight loss, ideally within a structured nutrition plan and physical activity program for cardiometabolic benefits **B** and histological improvement. **C**

4.15 For adults with type 2 diabetes particularly with overweight or obesity with nonalcoholic fatty liver disease, consider using a glucagon-like peptide 1 receptor agonist with demonstrated benefits in nonalcoholic steatohepatitis as an adjunctive therapy to lifestyle interventions for weight loss. **B**

4.16 Pioglitazone or glucagon-like peptide 1 receptor agonists are the preferred agents for the treatment of hyperglycemia in adults with type 2 diabetes with biopsy-proven nonalcoholic steatohepatitis, or those at high risk for nonalcoholic fatty liver disease with clinically significant liver fibrosis using noninvasive tests. **A**

4.17a In adults with type 2 diabetes and nonalcoholic steatohepatitis, use of glucose-lowering therapies other than pioglitazone or glucagon-like peptide 1 receptor agonists may be continued as clinically indicated, but these therapies lack evidence of benefit in nonalcoholic steatohepatitis. **B**

4.17b Insulin therapy is the preferred agent for the treatment of hyperglycemia in adults with type 2 diabetes with decompensated cirrhosis. **C**

4.18a Adults with type 2 diabetes and nonalcoholic fatty liver disease are at increased cardiovascular risk; therefore, comprehensive management of cardiovascular risk factors is recommended. **B**

4.18b Statin therapy is safe in adults with type 2 diabetes and compensated cirrhosis from nonalcoholic fatty liver disease and should be initiated or continued for cardiovascular risk reduction as clinically indicated. **B** Statin therapy should be used with caution and close monitoring in people with decompensated cirrhosis, given limited safety and efficacy data. **B**

4.19a Consider metabolic surgery in appropriate candidates as an option to treat nonalcoholic steatohepatitis in adults with type 2 diabetes and nonalcoholic steatohepatitis **B** and improve cardiovascular outcomes. **B**

4.19b Metabolic surgery should be used with caution in adults with type 2 diabetes with compensated cirrhosis from nonalcoholic fatty liver disease **B** and is not recommended in decompensated cirrhosis. **B**"

In the section "Assessment of Comorbidities," the text of the subsection "Nonalcoholic Fatty Liver Disease" has been revised as detailed below.

The following text has been added to the end of the paragraph about glucagon-like peptide 1 receptor agonists (GLP-1 RAs):

"The use of glucose-lowering agents other than pioglitazone or GLP-1 RAs may be continued in patients with type 2 diabetes and NAFLD for glycemic control, as clinically indicated. However, they have either failed to improve steatohepatitis in paired-biopsy studies (metformin) or have no RCTs with liver histological end points (i.e., sulfonylureas, glitinides, dipeptidyl peptidase 4 inhibitors, or acarbose)."

The following paragraphs have also been added to the section:

"Insulin is the preferred glucose-lowering agent for the treatment of hyperglycemia in adults with type 2 diabetes with decompensated cirrhosis given the lack of robust evidence about the safety and efficacy of oral agents and noninsulin injectables (i.e., GLP-1 RA, dual GLP-1/glucose-dependent insulinotropic polypeptide receptor agonist), although a recent 48-week study suggested that a GLP-1 RA may be safe in patients with nonalcoholic steatohepatitis (NASH) and compensated cirrhosis."

"A number of studies now recognize that adults with type 2 diabetes and NAFLD are at an increased risk of cardiovascular disease and require a comprehensive management of cardiovascular risk factors. Within a multidisciplinary approach, statin therapy should be initiated or continued for cardiovascular risk reduction as clinically indicated. Overall, its use appears to be safe in adults with type 2 diabetes and NASH, including in the presence of compensated cirrhosis (Child-Pugh class A or B cirrhosis) from NAFLD. Some studies even suggest that their use in people with chronic liver disease may reduce episodes of hepatic decompensation and/or overall mortality. Statin therapy is not recommended in decompensated cirrhosis given limited safety and efficacy data."

In line with the changes outlined above, additional minor revisions have been made to the section text for clarity and Table 4.1 and Fig. 4.2 have been revised as follows:

The laboratory evaluation section of Table 4.1, "Components of the comprehensive diabetes medical evaluation at initial, follow-up, and annual visits," has been revised to include "CBC with platelets" at the initial visit and annual visit.

The algorithm for risk stratification in individuals with NAFLD shown in Fig. 4.2 has been revised to remove NFS (NAFLD fibrosis score created by a group of experts that included American Diabetes Association representatives) as initial noninvasive testing for fibrosis and to specify the enhanced liver fibrosis blood test for additional risk stratification.

References

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