FEATURE ARTICLE

Screening for Metabolic Dysfunction–Associated Steatotic Liver Disease in Patients With Type 2 Diabetes: Are We Doing Enough?

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OBJECTIVE | Patients with type 2 diabetes are at an elevated risk for metabolic dysfunction–associated steatotic liver disease and advanced liver fibrosis. Multiple professional societies recommend initiating screening with a fibrosis-4 (FIB-4) index score calculation. This study aimed to evaluate the frequency of laboratory assessments necessary for FIB-4 score calculation in patients with type 2 diabetes.

RESEARCH DESIGN AND METHODS | A retrospective analysis of de-identified electronic medical records from 337,094 patients aged 40–75 years with type 2 diabetes was conducted to evaluate the completion rate of FIB-4 scoring and adherence to other recommended measurements and medications, including urinary albumin measurement and statin use.

RESULTS | Only 33% of patients with type 2 diabetes had all necessary components for FIB-4 score calculation, although this rate increased significantly over time (odds ratio 2.51, 95% CI 2.44–2.58) in the period from 2020 to April 2024 compared with 2010–2014. Urinary albumin measurements also increased but remained low at 13% during the period from 2020 to April 2024. Prescriptions for statin and newer antihyperglycemic medications significantly increased.

CONCLUSION | Our findings indicate that, although testing frequency for liver health in patients with type 2 diabetes is gradually increasing, substantial gaps in clinical practice persist.

Several professional societies (1,2) including the American Diabetes Association (ADA) (3) have recommended screening for advanced liver fibrosis in patients with type 2 diabetes. The rationale for this recommendation stems from the fact that patients with type 2 diabetes are at high risk for liver disease, with 65% having a greater than normal degree of liver steatosis (4), which is referred to as metabolic dysfunction–associated steatotic liver disease (MASLD). In addition, patients with comorbid type 2 diabetes and MASLD are at increased risk of developing advanced (stage 2–4) liver fibrosis, which in turn raises the risk for liver-related and all-cause mortality in patients with type 2 diabetes (5,6).

The ADA (3) and other professional societies (1,2) currently recommend a two-step screening strategy to identify advanced liver fibrosis in patients with type 2 diabetes. The first step involves calculating the fibrosis-4 (FIB-4) index score, which is derived from age, ALT, AST, and platelets. The second step triages patients based on FIB-4 score to further testing or referral to hepatology. Currently, rates of screening are uncertain across multiple settings, but there is a general belief that the FIB-4 index calculation should be readily available within electronic health record (EHR) systems because it can be calculated from available laboratory test values (7). We evaluated how frequently individuals with type 2 diabetes had an assessment of ALT, AST, and platelets to calculate a FIB-4 score. We also evaluated other metrics such as measurement of urinary albumin and the use of statins, which are generally recommended in patients with type 2 diabetes between the ages of 40 and 75 years (3,8).

Research Design and Methods

We identified patients with type 2 diabetes by ICD-10 codes using de-identified EHR records from a nationally representative patient population of >130 million U.S. adults as part of the Atropos Health Evidence Network's Eos database between 2010 to April 2024. The study population included

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patients who were 40–75 years of age with type 2 diabetes, with the first diagnosis of diabetes chosen as the index date. We also required two A1C measurements within 15 months after the index date (12 months plus a 3-month grace period), prescription of antihyperglycemic medication, and no history of liver disease (including ICD-10 codes for fatty liver, hepatitis, or cirrhosis). The frequency of the following tests within 15 months of the index date was assessed using standardized definitions based on the LOINC (Logical Observation Identifier Names and Codes) Ontology: ALT, AST, platelets, LDL cholesterol, triglyceride concentration, creatinine, and urinary albumin. We also evaluated prescriptions for statins and antihyperglycemic medications. We assessed three time periods (2010–2014, 2015–2019, and 2020 to April 2024) to understand differences in laboratory test ordering practices by time. The time period 2010–2014 was used as the reference group, and odds ratios (ORs) with 95% CIs were calculated after high-dimensional propensity score (hdPS) matching based on demographics, comorbid illnesses, and health care utilization (6). A propensity score model of the hdPS covariates is fitted using a logistic regression with LASSO (Least Absolute Shrinkage and Selection Operator) regularization that penalizes low weight (i.e., less contributory) variables down to zero weights such that the resulting parsimonious model has equivalent predictive performance without overfitting too many covariates in a high-dimensional setting (9,10). All analyses were performed using R, v. 4.2.1, statistical software.

Data and Resource Availability

The data that support the findings of this study are available from Atropos Health. Restrictions apply on the availability of these data, which were used under license for this study. Data are available from the authors with the permission of Atropos Health and its data providers.

Results

The patient population included 337,094 individuals with type 2 diabetes (mean age 58.9 years, 50.1% female, 34.2% White) (Table 1). Comorbid conditions such as hypertension and hyperlipidemia were prevalent, affecting 60% and 65% of patients, respectively. Metformin was the most common antihyperglycemic medication, prescribed for 56.2% of the population. Additionally, over half of the patients (56.9%) were prescribed a statin. As shown in Figure 1, half of the population had measurements of AST, ALT, or platelets, but only 33% had all components needed to calculate a FIB-4 score. Urine albumin was infrequently checked.

Figures 2 and 3 illustrate changes in laboratory measurements and medication prescriptions across the three time periods, and Table 2 presents the ORs and 95% CIs after hdPS matching. (See Supplementary Tables S1 and S2 for baseline characteristics after hdPS matching.) Compared with the reference period 2010–2014, laboratory assessments generally increased, with 42% of individuals having all components to calculate a FIB-4 score during the period from 2020 to April 2024 (OR 2.51, 95% CI 2.44–2.58, compared with 2010–2014). Measurement of urine albumin tripled from 2010–2014 to the period from 2020 to April 2024, but the proportion remained low (from 4.4 to 13%, OR 2.54, 95% CI 2.41–2.67). Medication utilization shifted, with a modest increase in statin prescriptions (from 47 to 64%, OR 1.69, 95% CI 1.65–1.74), and there was a marked increase in the use of newer antihyperglycemic medications such as glucagon-like peptide 1 (GLP-1) receptor agonists (OR 5.25) and sodium–glucose cotransporter 2 inhibitors (OR 9.52). Metformin use also increased modestly, while prescriptions of sulfonylureas and insulin decreased.

TABLE 1 Baseline Characteristics

	Individuals With Type 2 Diabetes (*N* = 337,094)
Age, years	58.9 ± 9.2
Female sex	168,774 (50.1)
Race	
Asian	7,266 (2.2)
Black	33,228 (9.9)
White	115,197 (34.2)
Other*	181,403 (53.8)
Hispanic ethnicity	25,252 (7.5)
Index years	
2010–2014	58,375 (17.3)
2015–2019	174,056 (51.6)
2020 to April 2024	104,663 (31)
Hypertension	203,242 (60.3)
Hyperlipidemia	219,653 (65.2)
Charlson Comorbidity Index	3.3 ± 1.9
Comorbidities	
Myocardial infarction	12,597 (3.7)
Cerebrovascular disease	18,790 (5.6)
Congestive heart failure	18,294 (5.4)
Peripheral vascular disease	16,554 (4.9)
Malignancy	19,703 (5.8)
Dementia	1,555 (0.5)
Antihyperglycemic medications	
Metformin	189,562 (56.2)
Insulin	103,182 (30.6)
Sulfonylurea	66,341 (19.7)
Dipeptidyl peptidase 4 inhibitor	41,853 (12.4)
Glucagon-like peptide 1 receptor agonist	40,197 (11.9)
Sodium–glucose cotransporter 2 inhibitor	34,629 (10.3)
Thiazolidinedione	13,636 (4.1)
Other	2,551 (0.8)
Statin medication	191,776 (56.9)

Data are reported as mean ± SD or *n* (%). *Other races included those not otherwise listed, mixed race, and unreported race.

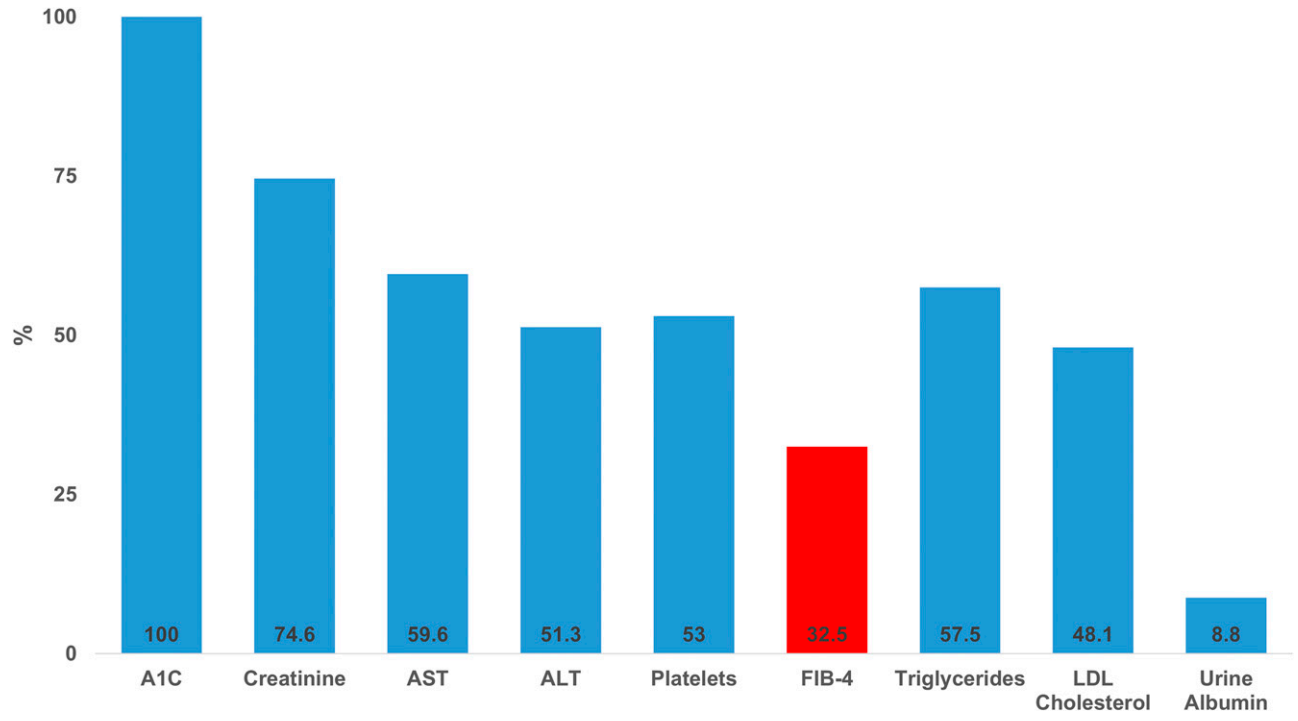

FIGURE 1 Percentages of patients with type 2 diabetes having recommended assessments.

Discussion

Our results suggest that a majority of patients with type 2 diabetes do not get routine blood testing to enable the calculation of a FIB-4 score. Although rates have been increasing since 2010–2014, 42% had all components to calculate a FIB-4 score. Thus, screening for advanced liver fibrosis will entail a change in practice that needs to include ordering platelets, AST, and ALT tests annually (Table 3).

Practice guidelines for patients with type 2 diabetes have met with variable success. Since 2015, the ADA has recommended

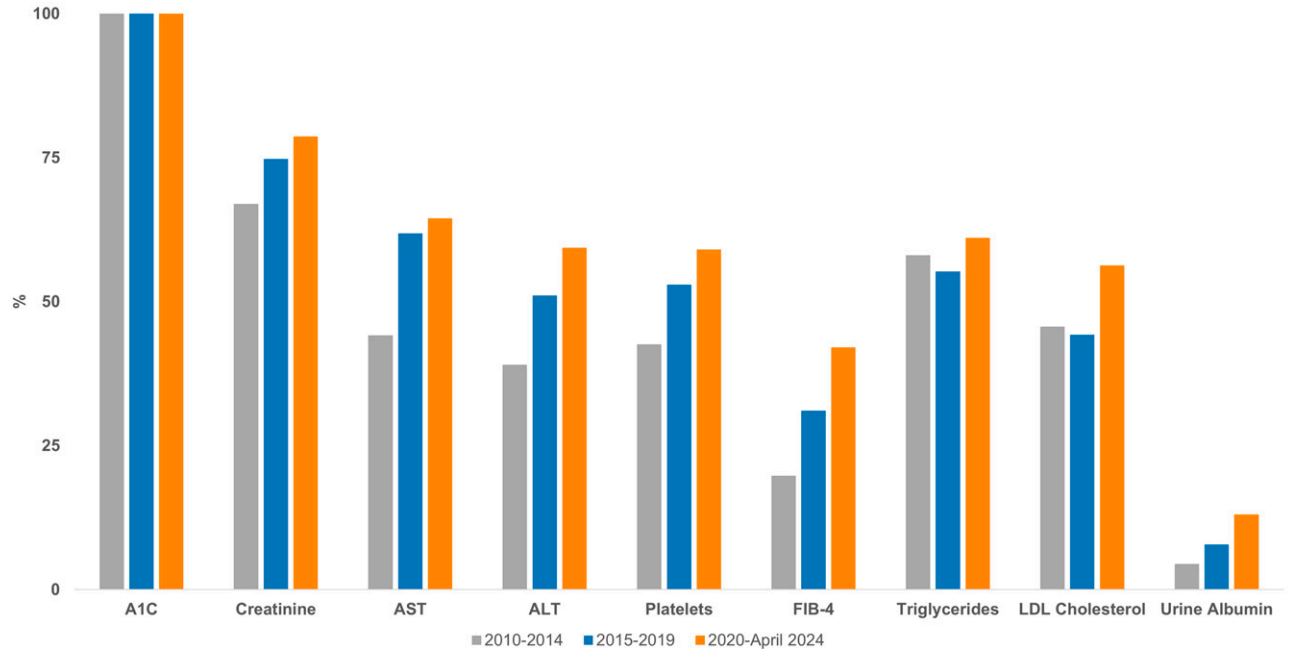

FIGURE 2 Changes in the percentage of patients with type 2 diabetes having recommended assessments by time period.

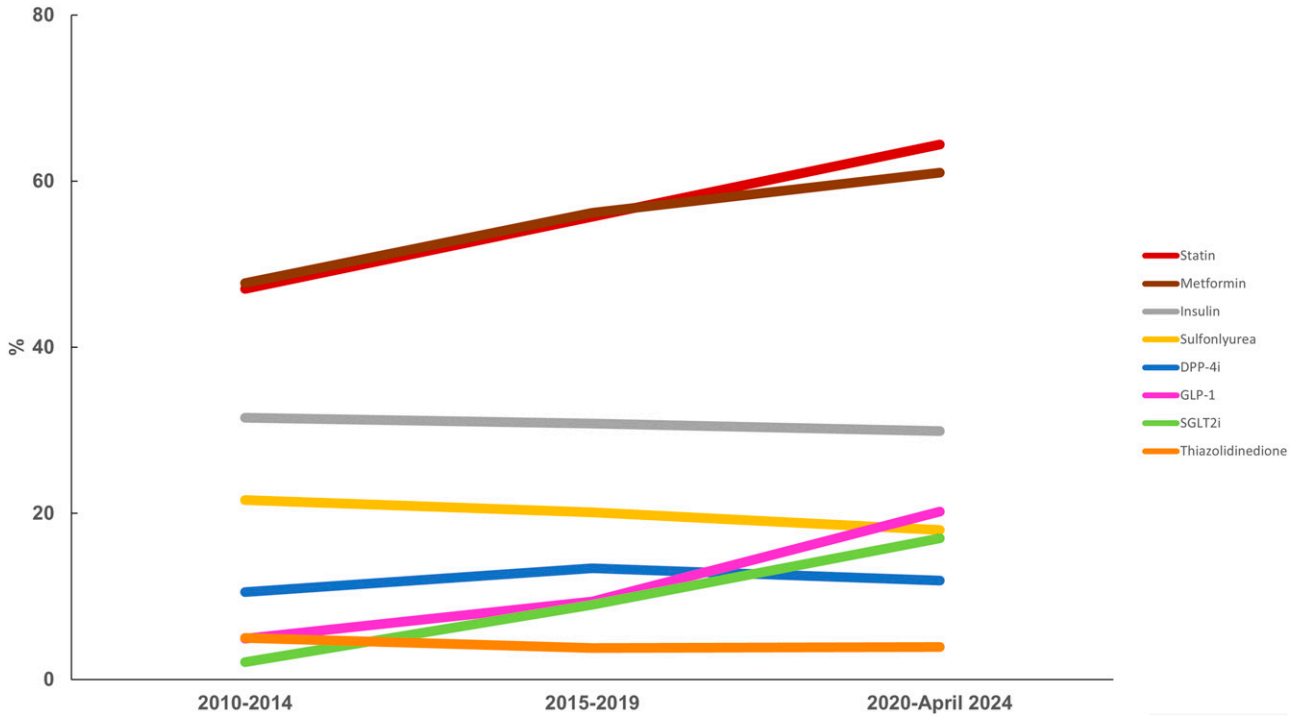

FIGURE 3 Changes in the percentage of patients with type 2 diabetes having recommended prescriptions for antihyperglycemic medications by time period. DPP-4i, dipeptidyl peptidase 4 inhibitor; GLP-1, glucagon-like peptide 1 receptor agonist; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

statins for all patients with diabetes aged 40–75 years regardless of LDL cholesterol concentration (11). Although statin use has increased (12), estimates suggest that ~50% of patients with type 2 diabetes use statins (13). In our study, statin use was found to have been increasing since 2010–2014, with 64% of patients with type 2 diabetes prescribed a statin in the past 4 years.

The ADA also recommends annual urinary albumin measurement in patients with type 2 diabetes (3). Although the proportion who had urinary albumin tripled, only 13% of patients with type 2 diabetes had this measurement in the period from 2020 to April 2024. A study in 2024 also found low rates of urinary albumin measurement (14.8%) in patients with type 2 diabetes aged 18–90 years in 20 health systems across the United States in the PCORnet database (14). Lower rates in our study may be secondary to the lower age range of patients included.

Unlike measuring urinary albumin, screening recommendations for advanced liver fibrosis include ordering several tests needed to calculate a FIB-4 score and stratifying patients by their FIB-4 score (3). Depending on the FIB-4 score, additional imaging (e.g., a FibroScan) and referral to hepatology may be warranted. Zhang et al. (15) showed that automating FIB-4 score calculations and creating electronic reminders for next steps significantly increased appropriate triaging of patients with high fibrosis scores from 3% in the control group to 33% in the intervention group. While this result was notable, only one-third of patients with increased fibrosis scores were appropriately referred for imaging or to hepatology. Thus, more concerted efforts may be required to increase appropriate screening for advanced liver fibrosis in type 2 diabetes.

Although several professional societies have recommended screening for advanced liver fibrosis in patients with type 2 diabetes (1–3), some have questioned the practicality of universal screening, citing poor sensitivity and specificity of the FIB-4 index, uncertain effect on patient management, and unclear long-term benefits of screening (16). The FIB-4 index has a sensitivity of 73% and specificity of 62%, and when combined with a test to measure liver stiffness, specificity of diagnosing advanced liver fibrosis can improve (17). Nevertheless, the current screening strategy may require ~40% of individuals with type 2 diabetes to have an imaging test and ~19% to be referred to a hepatologist (16). In addition to a large increase in health services with unclear cost-effectiveness, the survival benefits of this strategy remain unclear. Although there are doubts, approval of targeted therapies, such as resmetirom (18) for MASLD with moderate to advanced liver fibrosis in 2024, underline the importance of better

TABLE 2 OR (95% CI) of Selected Measurements and Medication Prescriptions Compared With Reference Time Period 2010–2014

	2010–2014	2015–2019	2020 to April 2024
Laboratory measurements			
AST	Reference	**1.94 (1.90–1.99)**	**2.23 (2.18–2.29)**
ALT	Reference	**1.57 (1.53–1.61)**	**2.10 (2.05–2.15)**
Platelets	Reference	**1.42 (1.39–1.46)**	**1.66 (1.62–1.70)**
FIB-4 score	Reference	**1.72 (1.67–1.77)**	**2.51 (2.44–2.58)**
Triglycerides	Reference	**0.87 (0.85–0.90)**	**1.06 (1.04–1.09)**
LDL cholesterol	Reference	**0.90 (0.88–0.93)**	**1.26 (1.23–1.30)**
Creatinine	Reference	**1.38 (1.35–1.42)**	**1.62 (1.58–1.67)**
Urine albumin	Reference	**1.66 (1.57–1.74)**	**2.54 (2.41–2.67)**
Medication prescriptions			
Statin	Reference	**1.39 (1.35–1.42)**	**1.69 (1.65–1.74)**
Metformin	Reference	**1.49 (1.45–1.52)**	**1.64 (1.60–1.68)**
Insulin	Reference	**1.04 (1.02–1.07)**	**0.94 (0.92–0.97)**
Sulfonylurea	Reference	0.98 (0.95–1.01)	**0.81 (0.78–0.83)**
Dipeptidyl peptidase 4 inhibitor	Reference	**1.38 (1.33–1.43)**	**1.06 (1.02–1.11)**
Glucagon-like peptide 1 receptor agonist	Reference	**2.24 (2.14–2.35)**	**5.25 (5.01–5.50)**
Sodium–glucose cotransporter 2 inhibitor	Reference	**5.13 (4.80–5.47)**	**9.52 (8.91–10.20)**
Thiazolidinedione	Reference	**0.80 (0.75–0.84)**	**0.79 (0.75–0.84)**

Data are OR (95% CI). Groups were compared after hdPS matching. See Supplementary Tables S1 and S2 for baseline characteristics after matching. Bold type indicates statistical significance.

identifying individuals with liver fibrosis. Newer antihyperglycemic medications such as GLP-1 receptor agonists also have been shown to reduce hepatic steatosis, improve steatohepatitis, and prevent major adverse liver outcomes such as cirrhosis (19,20). Our study indicates that the use of GLP-1 receptor agonists in patients with type 2 diabetes has quadrupled since 2010–2014, but the proportion remains low compared with the estimated 65% of people with type 2 diabetes with MASLD (4). Thus, management, as well as screening, of patients with MASLD needs intensification.

Limitations

Although we were able to evaluate a large patient population, our study has limitations. We may have misclassified some individuals because we relied on ICD-10 codes to identify individuals with type 2 diabetes. Nevertheless, all were on antihyperglycemic medications, and the study population was required to have two A1C measurements. Some patients may have had laboratory testing outside of the health care system, which is a common challenge in any retrospective EHR-based study. We addressed this concern by requiring two A1C values, enhancing the reliability of our laboratory data capture. Additionally, a medication prescription in an EHR may not indicate usage. However, determining medication usage was not the primary goal of this study.

Conclusion

The proportion of patients with type 2 diabetes getting laboratory tests to enable the calculation of a FIB-4 score has been increasing, but the proportion remains low. Although laboratory tests are necessary to calculate a FIB-4 score, active screening for MASLD requires an additional step of calculating the

TABLE 3 Practice Changes Needed to Facilitate MASLD Screening

Education	• Increase awareness of MASLD for providers and patients. ○ Over 65% of patients with type 2 diabetes are affected by MASLD, with >10% having advanced liver fibrosis (stage ≥2).
Physician-level action	• Order AST, ALT, and platelet counts annually to calculate FIB-4 score.
System-level action	• Implement an automated FIB-4 calculation within the EHR system.* • Develop or adopt a care pathway for MASLD management.*

*EHR-based calculators and pathways can be shared between institutions.

FIB-4 score and then triaging patients appropriately. Practice changes that could assist in facilitating MASLD screening are noted in Table 3. As therapies emerge for MASLD with fibrosis (21), systems need to be in place to allow risk stratification and appropriate identification of patients.

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DUALITY OF INTEREST

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AUTHOR CONTRIBUTIONS

S.H.K. wrote the first draft of the manuscript. S.H.K. and P.K. conceived and designed the study. G.H., C.W.P., and M.L.J. performed the statistical analyses. All authors interpreted the results, reviewed and edited the manuscript, and approved the final version. S.H.K. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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