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Review Article

Fatty Liver Index (FLI): Beyond a Marker of Hepatic Steatosis - A Comprehensive Review

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Abstract

Fatty liver disease is increasingly recognized as a significant global health issue, with non-alcoholic fatty liver disease (NAFLD) being the most common subtype. As the burden of NAFLD rises, accurate and accessible diagnostic tools are essential. The Fatty Liver Index (FLI) is a non-invasive biomarker that has been widely adopted for estimating hepatic steatosis based on routine clinical and biochemical parameters such as body mass index, waist circumference, triglycerides, and gamma-glutamyl transferase levels. Although initially developed to assess the presence of fatty liver, recent studies indicate that the FLI may hold value beyond diagnosing hepatic steatosis. It has been linked to metabolic syndrome, cardiovascular disease risk, and type 2 diabetes, suggesting its potential role as a broader metabolic health indicator. As research continues to explore the connections between liver fat accumulation and systemic diseases, FLI may emerge as a useful tool for early detection, risk stratification, and monitoring of metabolic disorders.

Introduction

Fatty liver disease, especially Non-Alcoholic Fatty Liver Disease (NAFLD), has gained recognition as one of the most common chronic liver conditions affecting populations globally. This condition arises due to the accumulation of fat within hepatocytes and is particularly prevalent in individuals with obesity, type 2 diabetes, and metabolic syndrome. NAFLD encompasses a spectrum of liver abnormalities, beginning with simple steatosis and potentially progressing to more severe forms, such as Non-Alcoholic Steatohepatitis (NASH), fibrosis, cirrhosis, and even hepatocellular carcinoma if left unmanaged [1,2].Traditionally, diagnosing hepatic steatosis relied heavily on invasive procedures, particularly liver biopsy, which, despite its diagnostic accuracy, carries risks and is not practical for large-scale screening or regular monitoring. In response to the need for safer and more accessible diagnostic tools, researchers have developed a variety of non-invasive indices. Among these, the Fatty Liver Index (FLI) has emerged as a widely accepted and validated marker for the presence of fatty liver [3].

Developed by Bedogni and colleagues, the FLI is a composite score that uses four easily obtainable clinical and biochemical variables: Body Mass Index (BMI), waist circumference, serum triglyceride levels, and gamma-glutamyl transferase (GGT) activity. These parameters, when combined using a specific algorithm, yield a score ranging from 0 to 100, with higher values indicating a greater likelihood of hepatic fat accumulation [4]. Generally, an FLI score below 30 suggests a low risk of fatty liver, while a score above 60 strongly indicates its presence.Initially introduced as a practical alternative to liver imaging or biopsy in the assessment of hepatic steatosis, the FLI is now being recognized for its broader clinical applications. Recent investigations have highlighted the utility of FLI beyond liver-related outcomes, particularly in identifying individuals at risk for metabolic complications [5]. Emphasized that elevated FLI scores are not only associated with liver fat but also correlate with markers of insulin resistance, systemic inflammation, and cardiovascular risk.The emerging evidence supports the integration of FLI into routine health assessments, especially for individuals with obesity or features of metabolic syndrome. It serves as a valuable screening tool for early detection of NAFLD and as a predictor of cardiometabolic disorders. Given its simplicity and cost-effectiveness, FLI can be employed in both clinical and research settings to monitor disease progression or the impact of therapeutic interventions such as lifestyle modifications, dietary changes, and pharmacologic treatment [6].

Role of the Fatty Liver Index (FLI) in Detecting Hepatic Steatosis

The Fatty Liver Index (FLI) has become an essential non-invasive tool in assessing liver fat accumulation, particularly in the diagnosis of hepatic steatosis. As a clinically validated surrogate marker, FLI provides a reliable estimate of the presence of fatty liver disease without the need for invasive procedures or costly imaging technologies. This index integrates four key parametersBody Mass Index (BMI), waist circumference, triglyceride levels, and gamma-glutamyl transferase (GGT)—to produce a

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score ranging from 0 to 100. This score reflects the likelihood of liver steatosis in an individual and can be used effectively in both clinical and research settings.Clinically, an FLI score of 60 or more is strongly suggestive of the presence of hepatic steatosis, while a score below 30 is typically used to rule out the condition with high confidence. Scores falling between 30 and 60 may warrant further investigation, depending on the individual's risk profile and other clinical indicators. This scoring system has been validated across multiple population groups and is now frequently utilized in large-scale epidemiological studies aimed at understanding the burden of liver disease.One of the major advantages of the FLI is its simplicity and accessibility. Traditional imaging methods such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) are effective in detecting liver fat but may be limited by availability, cost, and variability in interpretation. In contrast, the FLI relies on commonly available clinical data, making it a cost-effective and scalable option for widespread screening. This feature has been particularly valuable in large public health studies and for initial assessments in primary care settings [7-10].

Beyond its diagnostic role, the FLI has shown promise in predicting disease progression. It is increasingly recognized as not only an indicator of current liver fat accumulation but also a potential marker for future liver-related complications. Studies have demonstrated associations between elevated FLI scores and the development of more advanced liver conditions such as non-alcoholic steatohepatitis (NASH) and fibrosis. Furthermore, individuals with higher FLI values are more likely to exhibit features of metabolic syndrome, insulin resistance, and increased cardiovascular risk, emphasizing the systemic implications of liver fat accumulation.As the understanding of NAFLD continues to evolve, tools like the FLI are proving to be integral to early detection and long-term disease monitoring. Incorporating the FLI into routine health evaluations can aid in identifying at-risk individuals, guiding lifestyle and therapeutic interventions, and potentially improving patient outcomes. While further studies may help refine its use and thresholds in different populations, current evidence strongly supports the utility of the FLI as a practical and informative marker in the diagnosis and management of hepatic steatosis [11].

Advantages of FLI Over Traditional Diagnostic Methods

The Fatty Liver Index (FLI) offers several notable advantages over conventional diagnostic methods used for detecting hepatic steatosis. As a non-invasive, cost-effective, and widely accessible tool, FLI provides an efficient alternative to imaging techniques and liver biopsy, particularly in the context of large-scale screenings and primary care.Traditional imaging modalities such as ultrasound, Computed Tomography (CT), and Magnetic Resonance Imaging (MRI) are commonly used to detect fat accumulation in the liver. While effective, these methods are often expensive, may not be readily available in all healthcare settings, and require specialized equipment and trained personnel. Moreover, their use for routine or repeated screening is limited due to cost and logistical constraints, making them less suitable for broad public health applications.Liver biopsy, although still considered the gold standard for confirming hepatic steatosis and assessing inflammation or fibrosis, is invasive and carries potential risks. These include bleeding, infection, pain, and, in rare cases, more serious complications [12]. Additionally, biopsy sampling can be subject to variability due to the heterogeneous distribution of fat and fibrosis in the liver, potentially leading to sampling errors.

In contrast, FLI is calculated using easily obtainable clinical parametersBody Mass Index (BMI), waist circumference, serum triglycerides, and Gamma-Glutamyl Transferase (GGT) levels. These variables are routinely measured during standard health evaluations, making FLI highly accessible and convenient [13]. Its simplicity enables clinicians to screen large populations, identify individuals at risk of fatty liver disease, and initiate early lifestyle or therapeutic interventions without the need for specialized procedures.Given its practicality and strong predictive value, FLI represents a powerful tool for the early detection and monitoring of fatty liver disease, especially in settings where access to imaging or biopsy is limited [14].

FLI and Metabolic Syndrome

Non-Alcoholic Fatty Liver Disease (NAFLD) is increasingly acknowledged as the hepatic component of metabolic syndrome, a cluster of metabolic abnormalities that significantly heighten the risk of cardiovascular disease and type 2 diabetes. The Fatty Liver Index (FLI), initially developed to identify hepatic steatosis, has emerged as a valuable indicator of broader metabolic dysfunction. Numerous studies have demonstrated a strong association between elevated FLI scores and the individual components of metabolic syndrome, including insulin resistance, elevated triglycerides, low HDL cholesterol, central obesity, and hypertension.The correlation between FLI and metabolic syndrome is not only cross-sectional but also predictive. Elevated FLI has been shown to forecast the future development of metabolic syndrome in individuals who are initially free of the condition. This predictive capacity positions FLI as a valuable tool in early disease detection and preventative healthcare. For example, reported that higher FLI scores are significantly associated with incident metabolic syndrome over time, suggesting that FLI could be used not just for liver health assessment but also for broader metabolic risk stratification.Furthermore, as metabolic syndrome is a known precursor to type 2 diabetes and cardiovascular disease, using FLI as a screening tool in primary care settings may facilitate early intervention strategies. The non-invasive nature of FLI makes it particularly suitable for population-level assessments, allowing clinicians to identify high-risk individuals efficiently and initiate lifestyle or pharmacological interventions. As research continues to evolve, the role of FLI may expand beyond hepatology into endocrinology and cardiology, reinforcing its significance as a holistic marker of metabolic health [15-19].

Insulin Resistance and Diabetes

The Fatty Liver Index (FLI) has emerged as a valuable tool not only for detecting hepatic steatosis but also for identifying individuals at risk for insulin resistance and type 2 diabetes mellitus (T2DM). Numerous studies have highlighted a significant association between elevated FLI scores and insulin resistance, commonly measured using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). As insulin resistance is a hallmark feature of metabolic syndrome and an early indicator of T2DM risk, this relationship emphasizes FLI's clinical relevance beyond liver health.Individuals with higher FLI values often exhibit impaired glucose metabolism and elevated fasting insulin levels, suggesting that fatty liver and insulin resistance may share common pathophysiological pathways. Longitudinal research further supports this connection, revealing that elevated FLI can predict the onset of T2DM, even in individuals who initially present with normal glucose tolerance. These findings highlight the potential of FLI as a non-invasive and accessible marker for early diabetes risk assessment. The predictive value of FLI by demonstrating that individuals with high FLI scores were more likely to transition from prediabetes to full-blown diabetes over time. This predictive ability underscores FLI's utility in primary prevention strategies. Early identification of individuals with high FLI can prompt timely interventions, including lifestyle modifications and metabolic monitoring, aimed at halting the progression toward diabetes.Given the global rise in diabetes prevalence, incorporating FLI into routine screening protocols could enhance risk stratification and support proactive healthcare approaches. As research continues to validate its utility, FLI may become an integral component of comprehensive metabolic evaluations, bridging hepatology, endocrinology, and preventive medicine [20].

FLI and Obesity

Obesity is widely recognized as one of the most significant risk factors for the development of non-alcoholic fatty liver disease (NAFLD), with visceral adiposity being particularly impactful. The relationship between obesity and NAFLD is well-documented, as excess fat accumulation in the abdominal region is closely associated with the development of hepatic steatosis and its progression to more severe liver conditions such as non-alcoholic steatohepatitis (NASH). In this context, the Fatty Liver Index (FLI) has proven to be a valuable tool for identifying individuals at higher risk for NAFLD, particularly those with obesity.FLI has shown a strong correlation with body fat distribution, especially visceral fat, which is a key determinant of metabolic dysfunction and liver fat accumulation. Several studies have demonstrated that an increase in body mass index (BMI) and waist circumference is directly proportional to higher FLI scores. These measurements of central adiposity reflect the accumulation of fat in the abdominal region, a primary risk factor for both NAFLD and cardiovascular diseases.The ability of FLI to reflect obesity-related metabolic dysfunction further enhances its value as a screening tool. Elevated FLI scores are indicative of not only increased liver fat but also an underlying metabolic disturbance often linked to obesity. This makes FLI a reliable indicator for detecting early-stage NAFLD in obese individuals, allowing healthcare providers to implement early intervention strategies. Furthermore, the strong association between higher FLI and visceral adiposity provides clinicians with a non-invasive method for identifying individuals who may be at risk for developing obesity-related liver complications, such as NASH and liver fibrosis.Given the increasing global prevalence of obesity, incorporating FLI into routine clinical practice could improve early detection and personalized care for patients at risk of developing NAFLD, particularly in those with central obesity [21,22].

FLI and Lipid Profile

Dyslipidemia, which is commonly characterized by elevated triglycerides and low high-density lipoprotein (HDL) cholesterol levels, plays a central role in both metabolic syndrome and non-alcoholic fatty liver disease (NAFLD). These lipid abnormalities are closely linked to the development and progression of atherosclerosis, making them significant contributors to cardiovascular disease (CVD). Since the Fatty Liver Index (FLI) incorporates triglyceride levels as one of its key components, it naturally reflects lipid imbalances often seen in individuals with NAFLD and metabolic dysfunction.Studies have shown that elevated FLI scores correlate with increased levels of total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, highlighting the close connection between hepatic steatosis and lipid abnormalities. The index not only serves as a marker for liver fat but also reflects broader dyslipidemic conditions that contribute to cardiovascular risk. This dual functionality of FLI is particularly valuable as it can offer a more comprehensive screening tool for assessing both liver health and lipid metabolism.Given that dyslipidemia is a key risk factor for atherosclerosis and CVD, FLI could potentially serve as an effective non-invasive screening tool for lipid imbalances, in addition to detecting fatty liver. Elevated FLI could help identify individuals at higher risk of developing both liver diseases and cardiovascular complications, allowing for early interventions. By integrating FLI into routine assessments, clinicians could more effectively identify patients with lipid abnormalities and at higher risk for cardiovascular events, facilitating timely therapeutic measures to address both hepatic and cardiovascular health [23].

FLI and Cardiovascular Disease (CVD)

Non-alcoholic fatty liver disease (NAFLD) is not only a significant risk factor for liver-related complications but is also closely linked to an increased risk of cardiovascular events. Cardiovascular disease (CVD) remains the leading cause of mortality in patients with NAFLD, with individuals often developing arterial stiffness, subclinical atherosclerosis, and a heightened risk of myocardial infarction and stroke. The predictive value of the Fatty Liver Index (FLI) in forecasting cardiovascular outcomes, showcasing its role as an effective tool for early risk assessment. Elevated FLI scores are consistently associated with adverse cardiovascular outcomes, with studies suggesting that FLI may serve as an independent predictor of CVD-related mortality. The index's ability to reflect both liver fat accumulation and metabolic dysfunction means it can offer a comprehensive view of a patient's cardiovascular health. Specifically, high FLI values have been linked to increased arterial stiffness, which is a precursor to atherosclerosis and a major contributor to CVD risk. Furthermore, FLI has shown promise in identifying individuals at risk of developing myocardial infarction and stroke, as elevated scores are correlated with the presence of subclinical atherosclerotic lesions. This highlights the potential of FLI as a non-invasive biomarker for early identification of individuals who may benefit from cardiovascular interventions.As cardiovascular diseases continue to represent a major health burden, the use of FLI in clinical practice could significantly enhance the ability to identify at-risk patients before overt symptoms emerge. Early interventions in individuals with elevated FLI could lead to better management of both liver and cardiovascular health, ultimately improving long-term patient outcomes [24].

FLI and Hypertension

Hypertension, a central feature of metabolic syndrome, is frequently observed in individuals with high Fatty Liver Index (FLI) scores. Given that hypertension is a significant contributor to cardiovascular disease, the association between elevated FLI and increased blood pressure has garnered considerable attention. This correlation underscores the utility of FLI as an important marker for assessing cardiovascular risk, particularly in individuals who may be predisposed to developing hypertension and other related complications.Studies have consistently demonstrated that elevated FLI correlates with increased blood pressure levels, pointing to the impact of hepatic steatosis on systemic vascular function. The presence of fatty liver is often associated with a dysregulated metabolic profile that includes insulin resistance, dyslipidemia, and central obesity, all of which are known contributors to hypertension. Elevated FLI, which reflects fat accumulation in the liver, is thus an indirect indicator of these metabolic abnormalities. In fact, research suggests that individuals with high FLI scores are at a heightened risk for developing elevated blood pressure, which may, in turn, increase the risk for CVD and related mortality [25].

The relationship between FLI and hypertension is particularly significant given the bidirectional nature of the association. Hypertension not only contributes to the development of fatty liver but also exacerbates existing liver conditions, creating a vicious cycle. The link between FLI and blood pressure levels emphasizes the need for early detection and intervention. Elevated FLI could serve as a valuable tool for identifying individuals at risk of hypertension before clinical manifestations occur, providing an opportunity for preventative measures to be implemented. Integrating FLI into routine hypertension screening protocols could enhance cardiovascular risk stratification in the general population. By identifying individuals with both high FLI and elevated blood pressure, clinicians can better tailor interventions aimed at preventing the progression of CVD. This could include lifestyle modifications, such as dietary changes, increased physical activity, and, when necessary, pharmacological interventions. Moreover, managing both hepatic fat accumulation and hypertension concurrently may improve overall health outcomes and reduce the risk of developing severe cardiovascular complications, such as heart failure, stroke, and myocardial infarction. The correlation between FLI and hypertension highlights the broader implications of fatty liver disease in cardiovascular health. FLI could serve as a non-invasive, cost-effective marker for identifying individuals at risk for hypertension and CVD, ultimately contributing to better early intervention and long-term health management. By incorporating FLI into routine screening practices, healthcare providers could proactively address metabolic dysfunctions and reduce the burden of hypertension and cardiovascular diseases in at-risk populations.

FLI as a Prognostic Tool in Liver Disease Progression

Non-alcoholic fatty liver disease (NAFLD) has become a prominent global health concern, often progressing to more severe liver conditions such as fibrosis, cirrhosis, and even hepatocellular carcinoma (HCC). The Fatty Liver Index (FLI), a non-invasive biomarker, has been widely used to assess hepatic steatosis and has gained significant attention for its potential to predict the progression of liver disease. While primarily designed as a marker of hepatic fat accumulation, recent evidence suggests that FLI can also serve as a prognostic tool in evaluating liver disease severity and predicting future outcomes. Emerging studies, indicate that elevated FLI scores are associated with liver fibrosis, cirrhosis, and an increased risk of mortality, particularly due to metabolic and cardiovascular complications.

FLI and Liver Fibrosis

The progression from NAFLD to liver fibrosis is one of the major concerns associated with fatty liver disease. Liver fibrosis represents an intermediate stage of liver damage, and its severity significantly impacts patient outcomes. Without intervention, liver fibrosis can progress to cirrhosis, liver failure, and eventually hepatocellular carcinoma (HCC), which carries a poor prognosis. The ability to predict liver fibrosis early in the disease process is critical for timely intervention and preventing progression to advanced liver disease.

Several studies have shown that FLI scores are predictive of liver fibrosis, particularly in individuals with metabolic risk factors such as obesity, type 2 diabetes, and dyslipidemia. The index was found to have a high degree of sensitivity and specificity for identifying individuals with hepatic steatosis, and subsequent studies have suggested that elevated FLI scores may correlate with the presence of liver fibrosis.FLI provides an opportunity for early detection of liver fibrosis, especially when liver biopsy is not feasible due to cost, invasiveness, or patient concerns. Studies have shown that FLI overlaps with advanced fibrosis scores like the Fibrosis-4 (FIB-4) index and the NAFLD Fibrosis Score (NFS), which are commonly used to assess liver disease severity. The ability of FLI to mirror these more invasive scoring systems makes it an attractive alternative for liver disease staging. Early identification of individuals with high FLI scores could lead to lifestyle interventions, including weight loss, dietary changes, and exercise, aimed at preventing further liver damage and halting the progression to fibrosis.

FLI and Cirrhosis

As liver fibrosis progresses, cirrhosis becomes a critical concern, significantly increasing the risk of liver failure and complications such as ascites, variceal bleeding, and hepatic encephalopathy. Cirrhosis is the end-stage result of prolonged liver injury, and its development is often accompanied by irreversible liver damage. Therefore, the early detection of cirrhosis is essential for improving patient outcomes.FLI has shown promise as a non-invasive marker for identifying individuals at risk for cirrhosis, particularly when used in conjunction with other diagnostic tools. Although liver biopsy remains the gold standard for diagnosing cirrhosis, its invasiveness makes it unsuitable for routine screening. In contrast, FLI provides a quick and cost-effective alternative for identifying individuals at higher risk of cirrhosis. Elevated FLI scores have been linked to the presence of advanced liver fibrosis, which, if left unchecked, can eventually lead to cirrhosis. As such, FLI may serve as an important tool for identifying individuals who require more intensive monitoring for the development of cirrhosis and its complications.

FLI and Hepatocellular Carcinoma (HCC)

Hepatocellular carcinoma (HCC) is one of the most aggressive and fatal types of liver cancer, often arising in individuals with chronic liver disease. The development of HCC is closely linked to liver cirrhosis, and early detection is crucial for improving survival outcomes. While the role of FLI in predicting HCC is still under investigation, emerging data suggests that elevated FLI scores may be associated with an increased risk of HCC.A potential of FLI to predict the development of HCC in individuals with advanced liver disease. As FLI has been shown to correlate with liver fibrosis and cirrhosis, it is likely that its ability to identify individuals at risk for these conditions also extends to predicting HCC development. In individuals with a high FLI score, particularly those with a history of chronic liver disease or cirrhosis, the index could serve as an early warning system for the potential onset of liver cancer.

FLI and Mortality Prediction

Beyond its role in predicting liver disease progression, FLI has been identified as an independent predictor of all-cause mortality, particularly due to metabolic and cardiovascular complications. As fatty liver disease is closely linked to obesity, insulin resistance, dyslipidemia, and hypertension, individuals with high FLI scores are at an elevated risk for developing cardiovascular disease (CVD). Studies have shown that FLI is associated with subclinical atherosclerosis, arterial stiffness, and an increased risk of myocardial infarction and stroke.The association between FLI and cardiovascular risk underscores the importance of using FLI not only to monitor liver health but also to assess broader metabolic health. Elevated FLI scores can help identify individuals at risk for both liver disease and cardiovascular complications, allowing for early interventions aimed at reducing the overall burden of disease. In fact, some cohort studies have demonstrated that higher FLI scores are associated with an increased risk of mortality, particularly due to cardiovascular events.FLI has emerged as a valuable non-invasive tool for assessing liver disease severity and predicting disease progression in NAFLD. Its utility extends beyond the diagnosis of hepatic steatosis, providing important prognostic information about liver fibrosis, cirrhosis, and even hepatocellular carcinoma. As FLI is closely linked to metabolic dysfunction and cardiovascular risk, it offers a comprehensive approach to assessing the overall health of individuals with fatty liver disease. With its simplicity, accessibility, and cost-effectiveness, FLI holds great potential as a screening tool in both primary care and specialty settings. However, further research is needed to fully understand its prognostic value and refine its use in clinical practice. In the future, FLI could play a pivotal role in early disease detection, risk stratification, and personalized interventions, ultimately improving patient outcomes in individuals with fatty liver disease.

Limitations of FLI

While the Fatty Liver Index (FLI) has become an invaluable tool for diagnosing and predicting the progression of non-alcoholic fatty liver disease (NAFLD), it is not without its limitations. One significant drawback is its lack of specificity in distinguishing between different types of liver disorders, such as NAFLD and alcoholic liver disease (ALD). Both conditions share similar metabolic profiles and clinical manifestations, which makes it challenging to use FLI alone for accurate differentiation. In clinical practice, the potential overlap between these diseases means that FLI may not always provide definitive information, especially in patients with mixed etiologies of liver disease. Therefore, FLI should be used in conjunction with other diagnostic methods, such as liver biopsy, imaging techniques, or clinical history, to achieve a more comprehensive assessment of liver health. Another limitation of FLI is its inability to specifically identify liver fibrosis stages or the presence of cirrhosis. Although elevated FLI scores are associated with liver damage and disease progression, FLI does not offer detailed information about the degree of fibrosis or liver scarring. This is particularly important in NAFLD, where the progression to advanced stages, including cirrhosis and hepatocellular carcinoma (HCC), requires early and accurate detection. Although recent studies have suggested a correlation between high FLI scores and the presence of liver fibrosis, FLI alone cannot reliably assess the severity of liver injury. This limitation necessitates the use of additional biomarkers or advanced imaging techniques, such as elastography or magnetic resonance imaging (MRI), to provide more accurate information on liver fibrosis and cirrhosis.

Ethnic and genetic variations also play a role in FLI's accuracy. Research has shown that FLI may perform differently across various populations due to genetic and environmental factors that influence metabolic health. For instance, individuals from different ethnic backgrounds may have varying risk profiles for developing NAFLD and may exhibit differences in fat distribution, insulin resistance, and liver enzyme levels. This can impact the predictive value of FLI in diverse populations. For example, FLI may be less accurate in certain ethnic groups, where alternative diagnostic markers or population-specific adjustments may be necessary. Therefore, to maximize the effectiveness of FLI, it may need to be refined or adjusted for specific ethnic groups, ensuring that it provides reliable predictions for all individuals. Despite these limitations, FLI remains a valuable tool for identifying individuals at risk for NAFLD and for monitoring disease progression. However, to enhance its diagnostic power, there is a growing consensus that incorporating additional biomarkers and refining the algorithm may improve its predictive capabilities.

Future Perspectives

The future of liver disease diagnosis and risk stratification lies in the integration of various advanced technologies and biomarkers. One promising direction is the use of machine learning (ML) algorithms that can combine FLI with other genetic, clinical, and metabolomic data to create a more comprehensive risk assessment tool. Machine learning models have the potential to identify complex patterns within large datasets, leading to more accurate predictions of NAFLD progression and liver-related outcomes. By incorporating genetic markers associated with liver disease, along with metabolomic profiles, machine learning could refine the accuracy of FLI and help clinicians better predict disease trajectories and complications.Moreover, the growing field of personalized medicine offers additional opportunities to improve NAFLD risk stratification. Advances in genomics and precision medicine may allow for the development of more tailored approaches to NAFLD diagnosis and management. By identifying specific genetic variants or epigenetic changes that predispose individuals to NAFLD, researchers may be able to enhance FLI's predictive accuracy by integrating these markers into the algorithm. Personalized strategies based on genetic risk factors could enable earlier interventions, improving outcomes for patients at higher risk for liver disease progression.

Additionally, non-invasive biomarkers, such as serum markers, and advanced imaging modalities like elastography, MRI, or even artificial intelligence-based imaging techniques, are becoming increasingly important for the assessment of liver disease. These tools could complement FLI, allowing for a multimodal approach to NAFLD diagnosis and management. By integrating FLI with other emerging biomarkers and imaging technologies, clinicians will be better equipped to monitor liver disease in a more accurate and efficient manner, ultimately improving patient care.Furthermore, longitudinal studies are needed to better understand the predictive value of FLI in relation to long-term outcomes such as the development of cirrhosis or hepatocellular carcinoma. This will help in refining the thresholds of FLI for different stages of liver disease and in understanding how it can be integrated into broader clinical management strategies. For example, FLI could be used alongside other biomarkers to track disease progression over time and adjust treatment plans accordingly. While FLI is a valuable tool in the diagnosis and prediction of NAFLD, it has its limitations, including issues with specificity, variability across ethnic groups, and a lack of detailed information on liver fibrosis and cirrhosis. However, the future of liver disease diagnosis lies in the integration of FLI with other biomarkers, advanced imaging technologies, and machine learning algorithms, which will allow for more accurate risk stratification and personalized treatment plans. A multimodal approach incorporating FLI alongside emerging biomarkers and technologies could revolutionize the way liver diseases, including NAFLD, are diagnosed, monitored, and managed. This comprehensive approach holds great promise for improving patient outcomes and advancing the field of hepatology.

Discussion

The Fatty Liver Index (FLI) has emerged as a widely utilized non-invasive tool for the early diagnosis and monitoring of non-alcoholic fatty liver disease (NAFLD). Its primary strength lies in its simplicity, combining body mass index (BMI), waist circumference, triglyceride levels, and gamma-glutamyl transferase (GGT) to provide a reliable estimate of hepatic steatosis. However, as with any diagnostic marker, FLI has certain limitations, including its inability to differentiate between NAFLD and other liver disorders, such as alcoholic liver disease (ALD), and its lack of specificity in assessing liver fibrosis stages or the presence of cirrhosis. These limitations underscore the need for integrating FLI with other diagnostic methods, such as liver biopsy, elastography, or advanced imaging techniques, to provide a more comprehensive assessment of liver health.In recent years, the scope of FLI has expanded beyond hepatic steatosis detection, revealing its potential utility in predicting the progression of metabolic syndrome, cardiovascular disease (CVD), and other related conditions. Numerous studies, including those by Kaneva and Bojko (2024), have established correlations between elevated FLI and components of metabolic syndrome, such as insulin resistance, dyslipidemia, hypertension, and central obesity. This positions FLI as not only a tool for identifying liver disease but also as a valuable marker for identifying individuals at risk for developing broader metabolic disorders, including type 2 diabetes mellitus (T2DM) and cardiovascular events. This highlights the interconnectedness between liver dysfunction and systemic metabolic disturbances, reinforcing the importance of early detection and intervention.

FLI's association with cardiovascular outcomes is particularly noteworthy, as cardiovascular disease remains the leading cause of mortality among individuals with NAFLD. High FLI scores correlate with increased risks of arterial stiffness, subclinical atherosclerosis, and myocardial infarction, offering a predictive value beyond hepatic steatosis. This ability to serve as an independent predictor of cardiovascular mortality makes FLI a promising tool for risk stratification in individuals with metabolic risk factors, particularly in primary care settings where early identification of at-risk patients is crucial for preventing long-term complications.While FLI holds promise in assessing liver disease progression, it is important to note its limitations in accurately assessing liver fibrosis, a key factor in determining the severity of NAFLD. Although elevated FLI correlates with the presence of liver fibrosis, it cannot replace advanced scoring systems such as the NAFLD Fibrosis Score (NFS) or the Fibrosis-4 (FIB-4) index. Therefore, FLI should be viewed as part of a comprehensive diagnostic approach that includes other biomarkers and clinical evaluations.Emerging advancements in personalized medicine and machine learning algorithms may enhance FLI's predictive power by integrating additional biomarkers, genetic data, and metabolomic profiles. This approach holds the potential for refining FLI's accuracy, enabling more precise risk stratification for patients at various stages of liver disease. Moreover, combining FLI with new non-invasive biomarkers and imaging techniques will help clinicians monitor liver disease progression, improve treatment outcomes, and tailor interventions to individual patients.

Conclusion

The role of FLI provides significant utility in the diagnosis and monitoring of NAFLD, along with broader applications in assessing metabolic syndrome and cardiovascular risk. However, its limitations in fibrosis assessment and disease specificity necessitate its use in conjunction with other diagnostic methods. With the continued development of advanced technologies and multi-omic approaches, FLI may evolve into an even more powerful tool for the management of NAFLD and its associated comorbidities, ultimately leading to improved patient outcomes.

References

1. Kaneva AM, Bojko ER (2000) Fatty liver index (FLI): More than a marker of hepatic steatosis. J Physiol Biochem 80:11–26.
2. Abebe G, Ayanaw D, Ayelgn Mengstie T, Dessie G, Malik T (2002) Assessment of fatty liver and its correlation with glycemic control in patients with type 2 diabetes mellitus attending Dessie Comprehensive Specialized Hospital, Northeast Ethiopia. SAGE Open Med 10:20503121221124760.
3. Acosta FM, Sanchez-Delgado G, Martinez-Tellez B, Osuna-Prieto FJ, Mendez-Gutierrez A, et al. (2002) A larger brown fat volume and lower radiodensity are related to a greater cardiometabolic risk, especially in young men. Eur J Endocrinol 187:171–183.
4. Adamska A, Polak AM, Krentowska A, Lebkowska A, Hryniewicka J, et al. (2011) Increased serum fetuin-B concentration is associated with HOMA-β and indices of liver steatosis in women with polycystic ovary syndrome: a pilot study. Endocr Connect 8:1159–1167.
5. Ahmed AE, Ibrahim WA, Nabil ZM, Mansour KA, Mansour AMF, et al. (2002) Role of thymosin beta 4 in the diagnosis of nonalcoholic fatty liver and its relation to metabolic syndrome in Egyptian patients. Egypt J Immunol 29:76–86.
6. Ahn SH, Seo DH, Kim SH, Nam MS, Hong S (2008) The relationship between fatty liver index and bone mineral density in Koreans: KNHANES 2010–2011. Osteoporos Int 29:181–190.
7. Aizawa T, Nakasone Y, Murai N, Oka R, Nagasaka S, et al. (2002) Hepatic steatosis and high-normal fasting glucose as risk factors for incident prediabetes. J Endocr Soc 6:bvac110.
8. Amor AJ, Cofán M, Mateo-Gallego R, Cenarro A, Civeira F, et al. (2009) Dietary polyunsaturated fatty acids mediate the inverse association of stearoyl-CoA desaturase activity with the risk of fatty liver in dyslipidaemic individuals. Eur J Nutr 58:1561–1568.
9. Artaza JN, Norris KC (2009) Vitamin D reduces the expression of collagen and key profibrotic factors by inducing an antifibrotic phenotype in mesenchymal multipotent cells. J Endocrinol 200:207–221.
10. Balducci S, Cardelli P, Pugliese L, D'Errico V, Haxhi J, et al. (2015) Volume-dependent effect of supervised exercise training on fatty liver and visceral adiposity index in subjects with type 2 diabetes The Italian Diabetes Exercise Study (IDES). Diabetes Res Clin Pract 109:355-363.
11. Balkau B, Lange C, Vol S, Fumeron F, Bonnet F, et al. (2010) Nine-year incident diabetes is predicted by fatty liver indices: the French D.E.S.I.R. study. BMC Gastroenterol 10:56.
12. Barchetta I, Angelico F, Del Ben M, Baroni MG, Pozzilli P, et al. (2011) Strong association between non alcoholic fatty liver disease (NAFLD) and low 25(OH) vitamin D levels in an adult population with normal serum liver enzymes. BMC Med 9:85.
13. Barrea L, Annunziata G, Muscogiuri G, Di Somma C, Laudisio D, et al. (2008) Trimethylamine-N-oxide (TMAO) as novel potential biomarker of early predictors of metabolic syndrome. Nutrients 10:1971.
14. Barrea L, Macchia PE, Tarantino G, Di Somma C, Pane E, et al. (2015) Nutrition: a key environmental dietary factor in clinical severity and cardio-metabolic risk in psoriatic male patients evaluated by 7-day food-frequency questionnaire. J Transl Med 13:303.
15. Barrea L, Muscogiuri G, Modica R, Altieri B, Pugliese G, et al. (2001) Cardio-metabolic indices and metabolic syn-

drome as predictors of clinical severity of gastroenteropancreatic neuroendocrine tumors. Front Endocrinol 12:649496.

16. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, et al. (2006) The fatty liver index: A simple and accurate predictor of hepatic steatosis in the general population. BMC Gastroenterol 6:33.
17. Bellanti F, Lo Buglio A, Dobrakowski M, Kasperczyk A, Kasperczyk S, et al. (2002) Impact of sodium glucose cotransporter-2 inhibitors on liver steatosis/fibrosis/inflammation and redox balance in non-alcoholic fatty liver disease. World J Gastroenterol 28:3243–3257.
18. Bennet L, Groop L, Franks PW (2015) Country of birth modifies the association of fatty liver index with insulin action in Middle Eastern immigrants to Sweden. Diabetes Res Clin Pract 110:66–74.
19. Bonafini S, Tagetti A, Gaudino R, Cavarzere P, Montagnana M, et al. (2009) Individual fatty acids in erythrocyte membranes are associated with several features of the metabolic syndrome in obese children. Eur J Nutr 58:731–742.
20. Borges-Canha M, Neves JS, Mendonça F, Silva MM, Costa C, et al. (2001) The impact of vitamin D in non-alcoholic fatty liver disease: A cross-sectional study in patients with morbid obesity. Diabetes Metab Syndr Obes 14:487-495.
21. Borges-Canha M, Neves JS, Mendonça F, Silva MM, Costa C, et al. (2000) The impact of bariatric surgery on hepatic function and predictors of liver steatosis and fibrosis. Obes Surg 30:2935-2941.
22. Cantoral A, Contreras-Manzano A, Luna-Villa L, Batis C, Roldán-Valadez EA, et al. (2013) Dietary sources of fructose and its association with fatty liver in Mexican young adults. Nutrients 11:522.
23. Chang Y, Jeon J, Song TJ, Kim J (2002) Association between the fatty liver index and the risk of severe complications in COVID-19 patients: a nationwide retrospective cohort study. BMC Infect Dis 22:384.
24. Detopoulou P, Nomikos T, Fragopoulou E, Antonopoulou S (2001) Association of PAF and its metabolic enzymes with GGT and the fatty liver index in healthy volunteers. Curr Vasc Pharmacol 19:663–672.
25. Han AL, Lee HK (2002) Comparison of the diagnostic performance of steatosis indices for discrimination of CT-diagnosed metabolic dysfunction-associated fatty liver disease. Metabolites 12:664.