

ARTIFICIAL INTELLIGENCE FOR DETECTING AND QUANTIFYING STEATOTIC LIVER DISEASE

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Summary

The prevalence of hepatic steatosis is increasing globally. While non-invasive diagnostic methods like ultrasonography and clinical scoring systems have been suggested as alternatives to liver biopsy, their effectiveness has been questioned. Integrating Artificial Intelligence (AI) with traditional diagnostic methods is being explored to enhance the accuracy of non-invasive approaches. The research utilized science bibliographic databases for data retrieval, namely PubMed, Scopus, and Google Scholar. The search terms utilized were “fatty liver,” “hepatic steatosis” “artificial intelligent”, “machine learning”, “deep learning”, “convolutional neural network”, “artificial neural network” and “ultrasound” etc. The systematic review encompassed studies, which collectively demonstrated that AI had a notable impact on improving the diagnosis of various liver conditions including liver steatosis, steatohepatitis, liver fibrosis, and liver cirrhosis. Through qualitative analysis, it was found that AI was particularly effective in enhancing diagnostic accuracy for these conditions. The integration of AI-supported systems has shown promising advancements in the detection and quantification of steatosis, NASH, and liver fibrosis in patients with liver steatosis. These systems have demonstrated the ability to improve performance in accurately diagnosing and assessing the severity of liver diseases, providing healthcare professionals with valuable tools for more effective clinical management.

Keywords: artificial intelligence, deep learning, machine learning, fatty liver, ultrasound, hepatic steatosis

Rezumat

Inteligență artificială pentru detectarea și cuantificarea bolii ficatului steatozic

Prevalența steatozei hepatice este în creștere la nivel mondial. Deși metodele non-invazive de diagnostic, cum ar fi ultrasonografia și sistemele de scorificare clinică au fost sugerate ca alternative la biopsia hepatică, eficacitatea acestora a fost pusă sub semnul întrebării. Integrarea inteligenței artificiale (IA) cu metodele tradiționale de diagnosticare este în curs de explorare pentru a spori acuratețea abordărilor non-invazive. Cercetarea a utilizat baze de date bibliografice științifice PubMed, Scopus și Google Scholar. Termenii de căutare utilizați au fost „ficat gras”, „steatoză hepatică”, „inteligență artificială”, „învățare automată”, „învățare profundă”, „rețea neuronală convoluțională”, „rețea neuronală artificială” și „ultrasunete” etc. Review-ul sistematic a cuprins studii care au demonstrat că IA a avut un impact notabil asupra îmbunătățirii diagnosticului diferitelor afecțiuni hepatice, inclusiv a steatozei hepatice, steatohepatitei, fibrozei și cirozei hepatice. Prin intermediul analizei calitative s-a constatat că IA a fost deosebit de eficientă în îmbunătățirea acurateței diagnosticului

pentru aceste afecțiuni. Integrarea sistemelor susținute de IA a demonstrat progrese promițătoare în detectarea și cuantificarea steatozei, steatohepatitei și a fibrozei hepatice la pacienții cu steatoză hepatică. Aceste sisteme au demonstrat capacitatea de a îmbunătăți performanța în diagnosticarea și evaluarea cu acuratețe a severității bolilor hepatice, oferind profesioniștilor din domeniul sănătății instrumente valoroase pentru un management clinic mai eficient.

Cuvinte-cheie: inteligență artificială, învățare profundă, învățare automată, ficat gras, ultrasunete, steatoză hepatică

Резюме

Искусственный интеллект для выявления и количественной оценки жировой болезни печени

Распространенность стеатоза печени растет во всем мире. Неинвазивные методы диагностики, такие как ультразвуковое исследование и клинические балльные системы, были предложены в качестве альтернативы биопсии печени, однако их эффективность была поставлена под сомнение. В настоящее время изучается возможность интеграции искусственного интеллекта (ИИ) с традиционными методами диагностики для повышения точности неинвазивных подходов. Для поиска данных использовались научные библиографические базы данных: PubMed, Scopus и Google Scholar. В качестве поисковых терминов использовались «жировая дистрофия печени», «стеатоз печени», «искусственный интеллект», «машинное обучение», «глубокое обучение», «конволюционная нейронная сеть», «искусственная нейронная сеть», «ультразвук» и т. д. В систематический обзор вошли исследования, которые в совокупности показали, что ИИ оказывает заметное влияние на улучшение диагностики различных заболеваний печени, включая стеатоз печени, стеатогепатит, фиброз и цирроз печени. С помощью качественного анализа было установлено, что ИИ особенно эффективен для повышения точности диагностики этих состояний. Интеграция систем с поддержкой искусственного интеллекта показала многообещающий прогресс в обнаружении и количественной оценке стеатоза, стеатогепатита и фиброза печени у пациентов со стеатозом печени. Эти системы продемонстрировали способность повышать эффективность точной диагностики и оценки тяжести заболеваний печени, предоставляя медицинским работникам ценные инструменты для более эффективного клинического лечения.

Ключевые слова: искусственный интеллект, глубокое обучение, машинное обучение, жировая болезнь печени, ультразвуковое исследование, стеатоз печени

Introduction

Fatty liver disease is a condition characterized by fat accumulation in the liver, with two primary variants: alcoholic fatty liver disease and metabolic associated steatotic liver disease (MASLD). MASLD encompasses a spectrum of liver disorders characterized by fat accumulation in liver cells, typically observed in individuals who are overweight or obese [38]. MASLD can be further classified into simple fatty liver and metabolic associated steatohepatitis (MASH), which involves inflammation and hepatocellular injury [35]. On the other hand, alcoholic steatohepatitis is caused by excessive alcohol consumption, leading to inflammation and liver damage. This spectrum includes alcohol associated steatotic liver disease (ASLD), alcoholic hepatitis, and cirrhosis [8]. Elevated levels of liver fat are associated with an increased risk of serious health complications including diabetes, arterial hypertension, cirrhosis, kidney disease, and cardiovascular conditions [25].

It stands as one of the most prevalent chronic liver conditions globally, afflicting approximately 25% to 30% of adults [23]. The surge in fatty liver disease prevalence on a global scale is a cause for heightened concern. It is essential to recognize that the extent of this prevalence fluctuates significantly depending on the specific population under examination and the criteria utilized for diagnosis. Nevertheless, it is approximated that MASLD impacts a substantial portion of the world's population. In the United States, nearly half of those affected fall within the middle-aged demographic [7]. Moreover, projections suggest that a noteworthy percentage of newly identified MASLD cases may advance to MASH, with a subsequent subset progressing to serious complications such as cirrhosis or hepatocellular carcinoma (HCC). MASH stands as the foremost contributor to liver disease among individuals awaiting liver transplants in the United States. The core principle that connects MASLD to metabolic conditions like insulin resistance, dyslipidemia, and type 2 diabetes has been the subject of extensive academic investigation [36].

The progression of MASLD unfolds through four distinct stages. Starting with steatosis characterized by benign fat buildup in liver cells, it advances to MASH, involving liver inflammation. Continued inflammation can culminate in fibrosis, leading to the formation of scar tissue around the liver and neighboring blood vessels while still maintaining liver functionality. Cirrhosis, the most severe stage, arises from prolonged inflammation, resulting in liver shrinkage, scarring, and nodularity, with irreversible damage potentially leading to liver failure.

Healthcare professionals categorize MASLD severity into four classifications—normal, mild, intermediate, or severe—based on histological characteristics [8]. Timely identification and management can impede the advancement of MASLD and diminish liver fat accumulation. Nonetheless, with an anticipated surge in advanced liver diseases and related fatalities attributed to MASLD/MASH, efforts are imperative to curb the escalating MASLD prevalence and alleviate the burden of liver diseases [2]. The primary approach to treating MASLD and MASH involves lifestyle modifications such as dietary adjustments and physical exercise. Weight reduction has proven effective in tackling MASLD and MASH, showcasing a distinct correlation between specific nutrients and fatty liver disease [33].

Percutaneous liver biopsy has long been considered the gold standard for diagnosing liver diseases. This procedure provides crucial information such as confirmation of steatosis and quantification of fibrosis, ballooning, and lobular inflammation. Despite advancements in imaging techniques and non-invasive diagnostic methods, percutaneous liver biopsy remains an essential tool in the accurate diagnosis and management of liver diseases. Its ability to provide detailed information about the extent and nature of liver damage makes it indispensable in clinical practice. While newer technologies continue to emerge, the value of percutaneous liver biopsy in helping clinicians make informed decisions about patient care cannot be understated [5].

Abdominal ultrasonography serves as a commonplace and cost-effective method for diagnosing MASLD [30, 37]. While liver biopsy is employed to assess liver disease severity, it is an invasive procedure carrying risks such as hemoperitoneum or hemothorax, rendering it unsuitable for follow-up examinations [31]. Alternate diagnostic techniques including clinical/laboratory scores are subject to ongoing debates regarding efficacy. Magnetic resonance imaging proton density fat fraction (MRI-PDFF) is more precise albeit constrained by cost and availability [15]. Early-stage MASLD presents opportunities for improved diagnostic accuracy through transient elastography and specific biomarkers, with potential exploration of combining diagnostic strategies with artificial intelligence (AI) [42].

AI, a field within computer science, aspires to emulate human learning and problem-solving capabilities [9]. AI has made significant strides in various fields, with a notable impact in medical imaging. It encompasses expert systems founded on rule-based algorithms and machine learning (ML), a domain where patterns are discerned from data rather than predetermined rules [6]. ML encompasses unsu-

ervised, supervised, and reinforcement learning techniques which aid in uncovering distinctive traits, establishing associations between input-output pairs, and maximizing rewards respectively [26]. Incorporating AI with medical technologies has exhibited enhanced outcomes, reduced errors, and elevated care quality [21]. Studies have underscored the potential of such integration to revolutionize the landscape of diagnostic accuracy, treatment efficacy, and patient care standards.

Neural networks, inspired by the intricate structure of the human brain, comprise artificial neurons organized into layers, including hidden layers that transform input data. These networks simulate the functioning of biological neurons, processing inputs through weighted connections and non-linear functions. While early Artificial Neural Networks (AANs) had limitations in training depth, the evolution into Deep Neural Networks (DNNs) has overcome these challenges by utilizing multiple layers for complex tasks [17]. The rise of Convolutional Neural Networks (CNNs) in diagnostics has revolutionized image analysis, transitioning from expert-based to data-driven feature learning. Deep Learning (DL) techniques have enhanced accuracy and objectivity in medical image interpretation, particularly in diagnostic modalities like histopathology and medical imaging [24].

In the realm of liver imaging, AI applications have revolutionized the detection, characterization, staging, and treatment of liver disorders such as MASLD. Recent advancements in ultrasound (US) technology have particularly influenced the clinical outcomes for patients with MASLD, showcasing the potential of AI in enhancing diagnostic procedures. AI-driven diagnostic systems have demonstrated impressive precision, thanks to a range of algorithms commonly used such as support vector machines (SVMs), CNNs, multilayer perceptron, fuzzy Sugeno, and probabilistic neural networks (PNNs) [15].

The aim of this study is to evaluate the effectiveness of artificial intelligence-assisted diagnostic systems, especially in the context of steatotic liver diseases using imaging data, which may provide healthcare professionals with valuable tools for more effective clinical management.

Material and methods

In the research conducted, the bibliographic databases utilized were PubMed, Scopus, and Google Scholar. These databases were chosen for their comprehensive coverage of academic literature and their ability to provide access to a wide range of scholarly articles. Each database offers unique features and search capabilities that were instrumental in the compilation of relevant literature for the study. These

databases played a crucial role in the research process by providing access to a wealth of information and aiding in the development of a comprehensive understanding of the topic at hand. In conducting this study, the search terms utilized were specifically chosen to be relevant to: 1) the population under study - "fatty liver", "hepatic steatosis", "non-alcoholic fatty liver", "metabolic associated fatty liver disease", "metabolic associated steatotic liver disease" etc.); 2) first intervention group - "Artificial Intelligent", "Machine Learning", "Deep Learning", "Convolutional Neural Network", "Artificial Neural Network", etc.; 3) second intervention group - "Ultrasound", "Ultrasonography", "Sonography", etc.; 4) outcome - "Detect", "Quantify", "Diagnose", etc. Various studies have examined patients with hepatic steatosis, encompassing conditions such as MASLD, MASH, ASLD, and other disease stages. The interventions analyzed fell within the realm of AI and focused on computer vision (CV) for evaluating medical images, specifically US scans. These interventions aimed to identify and diagnose fatty liver disease and its progression.

Results and discussions

Diagnosis of liver steatosis

The integration of AI into US has shown to significantly improve diagnostic outcomes in the realm of fatty liver disease. However, it is crucial to acknowledge that variations in clinical input have contributed to increased heterogeneity within study results. These discrepancies could arise from differences in patient demographics, clinical environments, or diagnostic approaches utilized in the studies analyzed. The presence of such heterogeneity underscores the importance of understanding AI's performance within diverse clinical contexts. It emphasizes the necessity of considering the impact of these factors on diagnostic accuracy when implementing AI-assisted diagnostics. While AI integration with ultrasonography has brought about notable advancements due to the widespread availability and cost-effectiveness of ultrasound technology, it is important to note that human interpretation in ultrasonography analysis may introduce inconsistencies affecting diagnostic reliability [7]. This review affirms that the amalgamation of AI with ultrasonography mitigates human-related errors, leading to enhanced diagnostic precision. It advocates for the robustness and benefits of employing AI-assisted ultrasound in diagnosing steatotic liver disease. However, further clinical validation through randomized controlled trials comparing traditional imaging methods to AI-assisted systems is imperative to substantiate the performance disparities comprehensively. In summary, the seamless integration of AI with ultrasonog-

raphy holds promise in transforming the diagnostic landscape of fatty liver disease, but ongoing research and rigorous validation trials are essential to solidify its effectiveness in clinical practice.

More than 50 studies have explored various AI-assisted methods for diagnosing and staging hepatic steatosis, which have utilized diverse AI classifiers and feature extraction techniques, showcasing the versatility and effectiveness of DL algorithms in diagnosing liver steatosis from ultrasound images. In the last decade, there has been a growing focus on the application of AI in the study of liver steatosis, particularly for the analysis of large volumes of images aimed at detecting and classifying fatty liver disease. Notably, a study incorporating a Fuzzy neural network and advanced image processing techniques achieved a perfect accuracy of 100%, highlighting the significance of feature parameters in diagnostic accuracy [31]. CNN model designed for the automatic detection of fatty liver disease using B-mode ultrasound images. This model, by extracting steatosis-compatible features and employing a DL algorithm for image classification has achieved an impressive overall accuracy of 96.3%, surpassing the performance of traditional diagnostic methods [4]. The efficacy of integrating AI with ultrasonography for the diagnosis of steatosis, steatohepatitis and liver fibrosis, highlighting the superior performance of neural networks compared to non-neural network approaches [16, 20]. Studies focusing on categorizing the severity of hepatic steatosis have utilized expansive datasets comprising tens of thousands of ultrasound images, with even smaller datasets yielding high accuracy rates around 90% [18, 27 – 30, 41]. The effectiveness of DL models is primarily influenced by the feature extraction model rather than the AI classifier employed. While the prospects for automated diagnosis using DL algorithms appear promising, there remains a need for further development. The application of AI in the analysis of liver steatosis has shown immense promise in enhancing diagnostic accuracy and efficiency, paving the way for more advanced and reliable methods for the detection and classification of hepatic steatosis.

Diagnosis of fibrosis and steatohepatitis

Identifying the degree of fibrosis and the presence of hepatic steatosis is pivotal for tailoring patient management strategies and determining the appropriate interventions. Steatohepatitis characterized by inflammation and hepatocellular injury signifies a higher risk of disease progression and complications, making its accurate diagnosis crucial for timely therapeutic measures. The potential of AI in diagnosing steatohepatitis appears encouraging, demonstrating a satisfactory sensitivity level.

However, it's crucial to acknowledge the variability observed, influenced by diverse populations and diagnostic methods, which highlights the need for more extensive research. The scarcity of studies emphasizes the importance of intensifying research endeavors to broaden the range of investigations, facilitating more thorough and dependable analyses.

A variable proportion of individuals diagnosed with MASLD develop MASH, which can progress to fibrotic changes in the liver. The development of fibrosis is a gradual process, but some patients may present with advanced liver disease and fibrosis, which is a major determinant of prognosis in MASLD. The risk of all-cause and liver-related mortality rises with the advancement of fibrosis stages in MASLD patients [10]. Therefore, precise non-invasive tests for assessing fibrosis are crucial in reducing the incidence of liver cirrhosis and HCC.

Assessing the level of liver fibrosis is crucial when evaluating patients with hepatic steatosis, and non-invasive techniques like real-time elastography (RTE) or shear-wave elastography (SWE) are widely utilized as alternatives to liver biopsies. A recent meta-analysis found that both point SWE (pSWE) and transient elastography exhibit comparable accuracies in identifying significant fibrosis, advanced fibrosis, and cirrhosis among MASLD patients. Despite limitations in obese patients, two dimensional SWE (2D SWE) has demonstrated feasibility even in severely obese individuals, with a high success rate of 97.3% and correlations with body mass index (BMI), waist circumference, nonalcoholic fatty liver disease activity score, and steatosis in univariate analysis. Moreover, transient elastography, 2D SWE, and MRI demonstrate similar diagnostic accuracies, particularly for significant and advanced fibrosis in MASLD patients with confirmed biopsies. Multiparametric ultrasound techniques, which include measures like dispersion slope, attenuation coefficient, and shear-wave speed, enable the differentiation of inflammation, steatosis, and fibrosis stages in MASLD patients. The incorporation of attenuation imaging signifies a notable advancement in ultrasound technology for accurately assessing liver fibrosis and steatosis in MASLD patients. Automated AI and DL analysis utilizing CNNs can greatly assist medical professionals in accurately classifying and staging conditions such as inflammation, steatosis, and fibrosis using non-invasive ultrasound techniques. These techniques are not only highly accurate but also cost-effective and widely accessible in primary care or point-of-care settings. The effectiveness of AI-supported ultrasonography and elastography, as well as CT, MRI, and clinical parameters have been demonstrated, particularly for diagnosing

liver steatosis and significant accuracy was observed for detecting advanced fibrosis and liver cirrhosis, showcasing the potential of AI-driven analysis in enhancing diagnostic capabilities.

Diagnosis of advanced steatotic liver disease

The rapid advancement of non-invasive modalities for assessing fibrosis and steatosis in chronic liver diseases is paving the way for more precise clinical decision-making algorithms [11]. Recent data suggests the utility of a “rule of five” for Liver Stiffness Measurements (LSMs) using Vibration-Controlled Transient Elastography (VCTE) and a “rule of four” for LSMs with Acoustic Radiation Force Impulse (ARFI) techniques in distinguishing different fibrosis stages [34].

In patients with advanced chronic liver disease (CLD), higher liver stiffness values are associated with an increased risk of liver decompensation, making SWE a promising predictor of morbidity and mortality in those with cirrhosis [12]. Both VCTE and ARFI techniques have shown effectiveness in non-invasive screening for varices, while LSM measurements are now integrated into predictive algorithms for HCC occurrence in high-risk populations with CLD [13, 14]. Moving forward, the inclusion of AI and DL/ML techniques seems inevitable in the field of assessing CLD. Traditional methods such as ANNs and grayscale imaging patterns have paved the way for assessing liver conditions over the past 25 years. These techniques have since evolved to incorporate Doppler information from color flow and pulsed Doppler measurements, enabling the development of ANN models that can quantify advanced liver fibrosis and cirrhosis with high accuracy [40]. Moreover, the integration of multiple serological tests and LSMs into diagnostic models further enhances the diagnosis of cirrhosis, significant portal hypertension, and esophageal varices, boasting an estimated accuracy rate exceeding 80% [32]. With the abundance of non-invasive markers available for risk prediction in chronic liver diseases, it is evident that AI and DL/ML techniques will play an increasingly pivotal role in the future assessment of these complex conditions.

DL approaches have seen significant advancements, particularly in the realm of automatic liver fibrosis classification, surpassing traditional non-deep learning algorithms such as artificial neural networks, multinomial logistic regression, support vector machines, and random forests [39]. Studies have showcased the efficacy of CNNs in achieving higher areas under the receiver operating characteristic curve (up to 0.85–0.95) for scoring liver fibrosis stages.

ML has also proven value in predicting bleeding esophageal varices in advanced CLD. An AI algorithm leveraging extreme-gradient boosting [1] based on laboratory measurements and LSM achieved

an impressive 98.7% accuracy in predicting variceal bleeding, surpassing endoscopic classification alone. The multicentric ML-based approach aimed to predict high-risk varices in compensated cirrhosis to mitigate unnecessary endoscopies [19] and successfully predicted portal vein thrombosis (PVT) post-splenectomy in portal hypertension patients. These advancements underscore the utility of DL and ML in enhancing diagnostic capabilities and treatment outcomes in liver-related conditions [22].

Conclusion

The progression from traditional approaches to feature learning through AI has significantly improved medical image diagnosis, especially in liver-related conditions like MASLD, underscoring the transformative impact of AI technologies in healthcare. Medical imaging research data strongly supports the integration of AI within healthcare settings, particularly in enhancing early-stage MASLD diagnosis, precise quantification of MASLD, and accurate estimation of liver fibrosis stages. This implementation aims to reduce subjectivity, minimize human errors, and introduce computer-aided diagnosis for less experienced medical professionals. The future potential lies in combining AI techniques with ultrasound to aid clinical decision-making in managing MASLD patients.

Despite growing interest, there are currently only a limited number of clinically approved AI applications for MASLD diagnosis and prognosis. The next steps involve conducting larger studies with external validation, improving healthcare infrastructure, and focusing on creating models that address challenges through randomized clinical trials on substantial patient cohorts. These efforts will contribute to the advancement of explainable AI and the development of more accurate image processing techniques for precise staging. Moreover, comparing computational complexity and classification accuracy between DL and ML methods will facilitate the selection of optimal approaches for detecting and quantifying MASLD using ultrasound images.

Declaration of conflict of interest

No conflict of interest.

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