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Contents

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MINIREVIEWS

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Contents

ABOUT COVER

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AIMS AND SCOPE

The primary aim of *Artificial Intelligence in Gastroenterology* (*AIG*, *Artif Intell Gastroenterol*) is to provide scholars and readers from various fields of artificial intelligence in gastroenterology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIG mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastroenterology and covering a wide range of topics, including artificial intelligence in gastrointestinal cancer, liver cancer, pancreatic cancer, hepatitis B, hepatitis C, nonalcoholic fatty liver disease, inflammatory bowel disease, irritable bowel syndrome, and *Helicobacter pylori* infection.

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MINIREVIEWS

Artificial intelligence for cancer detection in upper gastrointestinal endoscopy, current status, and future aspirations

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Abstract

This minireview discusses the benefits and pitfalls of machine learning, and artificial intelligence in upper gastrointestinal endoscopy for the detection and characterization of neoplasms. We have reviewed the literature for relevant publications on the topic using PubMed, IEEE, Science Direct, and Google Scholar databases. We discussed the phases of machine learning and the importance of advanced imaging techniques in upper gastrointestinal endoscopy and its association with artificial intelligence.

Key Words: Artificial intelligence; Upper gastrointestinal endoscopy; Esophageal cancer, Gastric cancer, Barrett's esophagus

Core Tip: This minireview aims to explore an important topic; the role of artificial intelligence in upper gastrointestinal (GI) endoscopy detection of cancer. We tried to delineate the most common obstacles encountered when trying to implement artificial intelligence in upper GI endoscopy for cancer detection and characterization. Moreover, we tried to outline the future prospects of this technique, along with its benefits, and uncertainties. This topic summarizes the wide scope for integration of

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artificial intelligence, between the practicing physicians and the computational engineers and how their collaboration could provide a better healthcare services.

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INTRODUCTION

Upper gastrointestinal (GI) cancers affecting the esophagus and stomach are responsible for more than one and half million annual deaths worldwide. Both are considered aggressive cancers, discovered mostly at an advanced stage, when curative measures are no longer applicable[1].

The current standard method for diagnosis of upper GI cancers is upper GI endoscopy and biopsy, using a white light endoscopy. The most common upper GI cancers encountered are esophageal adenocarcinoma, Barrett's esophagus (BE) and gastric cancer[2]. Artificial intelligence (AI) could add more accuracy to early cancerous and precancerous lesion detection in the upper GI during endoscopic evaluation[3].

Regardless of the great progress of AI in colonoscopy examinations, the integration of AI in upper GI endoscopy is still a new area of research with only a few pilot studies available, mostly due to unavailability of large datasets annotating upper GI cancers[2].

A recent meta-analysis examined the effect of AI in detecting *Helicobacter pylori* (*H. pylori*) infection during upper GI endoscopy, and found eight studies with pooled sensitivity of 87%, and specificity of 86%[4]. Moreover, another study combined the effect of neoplasm detection and *H. pylori* infection status, and found twenty-three studies with high pooled diagnostic accuracy in upper GI neoplasms; 96 in gastric cancer, 96% in BE, 88% in squamous esophagus and 92% in *H. pylori* detection[5].

IMPORTANCE OF USING AI IN UPPER GI ENDOSCOPY

The miss rate of detecting upper GI cancers reaches 11.3% according to a meta-analysis by Menon and Trudgill[6], and even higher rates could be observed in superficial neoplasms, reaching 75% (*i.e.*, gastric superficial neoplasia)[7]. According to a recent meta-analysis by Arribas *et al*[3], using AI integrated upper GI endoscopy yielded pooled sensitivity of 90%, and specificity of 89% for detection of neoplastic lesions, independent of the type of neoplasia (whether esophageal adenocarcinoma, BE, or gastric adenocarcinoma).

Expert sensitivity and specificity criteria in detecting the upper GI tumors differ from the detection and characterization of colorectal polyps for a few reasons. First, due to over-specialization of certain types of upper GI cancers according to the geographical prevalence of the cancer, for example, in the gastroenterologist's practice, resulting in limited training for the detection of non-prevalent types of cancers. AI integrated systems don't suffer the same geographical bias, thus offering better detection independent of the prevalence of GI cancer types[3]. Colon cancer prevalence is higher, enabling more data storage and more training.

The second reason, lesions that are minimal (in size or in depth) or hard to visualize by the inexperienced endoscopist, could be easily detected using the AI assistance[2]. Furthermore, gastric cancer lesions can be masked after eradication of *H. pylori*, this masking is due to regression of the mucosal elevation (decrease in its height) caused by the regression of chronic inflammatory process of *H. pylori* infection, or due to the coverage of the neoplastic area with atypical mucosa or even healthy columnar mucosa[8,9]. Advanced imaging techniques[10], when associated with AI, might help in detection of these masked neoplastic lesions.

Third reason being that training is not adequate in postgraduate courses, either because of insufficient interest (due to different cancer prevalence), or insufficient resources (especially for the computer simulation programs)[11]. However, an AI cumulative sensitivity of 91% for early-stage neoplasia proves that AI integrated systems will increase the efficacy of diagnostic upper GI endoscopy immensely. Thus, there is an urgent need for AI implementation in the clinical setting, even more urgent than the lower GI colonoscopy. Diagnostic settings have the issue of less experienced endoscopists compared to intervention intended settings, so early cancerous lesions tend to be easily overlooked (undetected)[3]. This of course will not eliminate the need for experienced endoscopists; however, integration with AI will have the best yield [12], considering that most of the upper GI lesions are non-polypoid which require higher level of skills for detection than colorectal cancer.

AI IN UPPER GI ENDOSCOPY

Machine learning (ML) must pass through multiple phases for validation in both training and testing (as shown in Figure 1). The AI used in endoscopy is ML, the most prevalent type of ML is deep learning (DL).

The first wave of AI was logic based handcrafted knowledge. In this logic-based handcrafted algorithms were developed separately for each task. This allowed the reasoning behind decisions of the first wave to be quite high, because every step of decision was handcrafted. However, the machine was unable to learn. The second wave of AI (the current wave) is the statistical ML in which the machines can learn from data, with an easily implemented learning algorithm, to generate a model used to carry out decisions. This eliminates the difficult part of designing and implementing a task-specific algorithm. While this raised the level of ML, it also caused a huge decline in the reasoning for the decisions. This means that the reasoning behind a wrong decision becomes hard to identify, rendering the algorithm a black box. The best way to avoid highly wrong decision rates is for provide a large amount of variable data to the machine to learn from[13].

ML passes through many phases. First phase is the training phase; where an annotated dataset is used to train the ML system, and then validated by determining the number of images it correctly identified. Second is the testing phase where a non-annotated dataset is given to the ML system to examine its diagnostic capabilities in comparison to experts in the field, and then using this ML system in a clinical setting, either in real time or in prospective trials to evaluate its performance in a real-world clinical setting.

There are two types of gastric lesion examinations identified during upper GI endoscopy using AI: (as shown in Figure 2): (1) Lesion detection (to know whether it is present or absent) and localization (to know its exact location in the GI tract); and (2) Lesion characterization (to assess its histological prediction).

The first type uses images with low or moderate quality, but the second type uses advanced optical diagnostic tools including: Narrow band imaging (NBI), chromoendoscopy, endocytoscopy, optical magnification, among others[14,15]. All types use semi-automatic identification, where the endoscopist delineates the affected area and centers the polyp near the endoscope lens for better visualization[14]. Invasion depth has been successfully predicted (with 89% diagnostic accuracy) through coding systems that are not very complicated, a proposed implementation of automated DL models in gastric cancers. Furthermore, another proposed implementation of a modified version by the same author is faster by 13 min in the test stage on unknown data, but has a slightly lower accuracy of 82%, with similar performance to experts and higher than trainees[16].

CURRENT STATUS, WHAT IS ACHIEVED AND WHAT IS NOT

If feasibility and usefulness of non-real time can be proved, then technical feasibility of real time is achievable, with an increased degree of sophistication of implementation and cost. Improvement of this real time feasibility could be accomplished through software programming of graphic processing unit (GPU) and central processing unit (CPU), along with implementation of specialized hardware systems.

Most implementations in AI use DL algorithms such as convolutional neural network (CNN). Wu *et al*[17] did the only randomized controlled trial (RCT) available on the topic. The team examined the diagnostic accuracy of their AI system using a

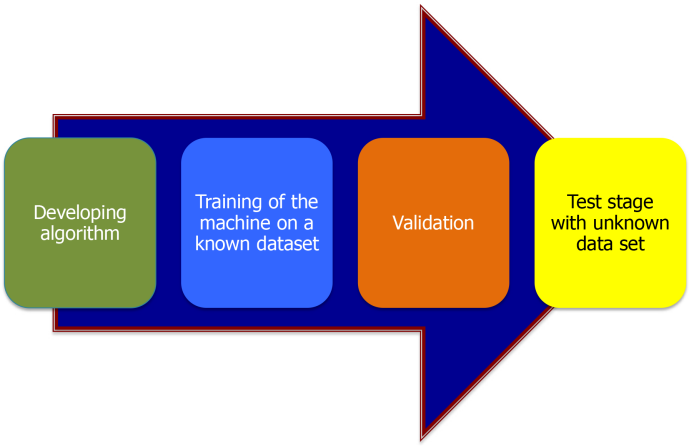

Figure 1 Showing the phases of machine learning.

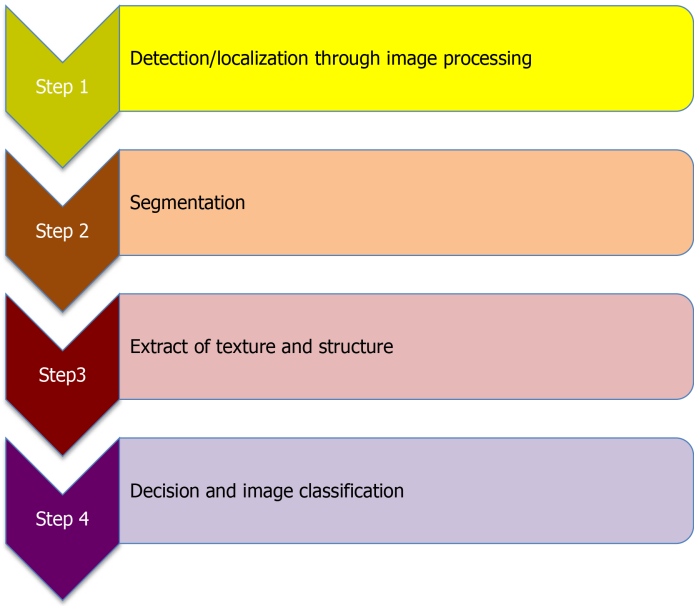

Figure 2 Showing the Step manner approach from detection to characterization.

deep convolution neural network. The system aimed to decrease the blind spots during upper GI endoscopy[17]. Unfortunately, they only examined images of benign and malignant lesions, not during a real time endoscopy performance.

Comparing white light alone *vs* linked color imaging showed that endoscopists had a lower miss rate with linked color imaging (30.7% *vs* 64.9%) in detecting early gastric cancers post-*H. pylori* eradication[18]. Linked color imaging is a technique that enhances the color range and brightness of images, developed by Fujifilm, Tokyo, Japan[19].

White light for detection of upper GI neoplasms is the most common and the standard technique. Other methods using advanced high-quality imaging are becoming increasingly available in most endoscopy centers. These advanced imaging techniques increase the sensitivity and specificity of diagnostic accuracy, especially in BE. There is a noticed "synergy" between AI integrated systems and advanced imaging techniques. On the other hand, the bias in having good quality images is apparent when identifying artifacts and lighting errors as cancerous lesions, or as called "spectrum bias" (this is a systematic error, where the data used do not represent the patients in question). This is equal in AI and humans[20,21].

While, dye-based imaging enhanced endoscopy (IEE) uses a dye to enhance detection of neoplastic lesions, this might not be helpful for examining a wide tract for lesions, nor for spraying the whole GI tract with dye. However, equipment enhanced IEE (eIEE) solves these problems. eIEE was originally classified into lightening-only

techniques along with blue laser imaging (BLI), BLI-bright and NBI (Olympus), autofluorescence imaging (Olympus), and post-processing-only techniques such as: Flexible spectral image color enhancement - (Fujifilm) and iSCAN - (Pentax), all from Tokyo, Japan[22,23].

LCI merges the two techniques by low frequency intensity light, red color extraction, and variation enhancement in a red-green-blue color space digital image post-processing. The post-processing system has three modes of color enhancement (A, B and C) with varying grades. This yields enhancement of hemoglobin-related information and neoplastic lesion in C2 and C3 modes or enhancement of neoplastic structures in B7 and B8[10].

The visualization using a NBI was mostly used to detect the histological features in the research studies. NBI is an advanced imaging technology that uses digital optical methods to visualize more enhanced images than the standard white light[24]. NBI helps to examine the vascularity and abnormal histological features on site during colposcopy, thus adding AI to narrow band could improve the detection of the exact histology of polyps and saves time and effort waiting for histopathological assessment that may delay the intervention[25]. In addition, the NBI technique is easier than other more sophisticated techniques as chromoendoscopy[26].

Shin *et al*[27] used high resolution microendoscopy to detect esophageal cancer using AI integration, showing sensitivity of 93% and specificity of 92% in the training set and similar results, albeit slightly lower, in the test and independent sets.

Moreover, in other techniques like, capsule endoscopy, images taken couldn't be adjusted in position lightening or quality as they are dependent mainly on gut motility, plus their role in upper GI tract evaluation is still limited[28,29].

Online processing causes limitation on the acceptable latency requiring it to be low, so real time application mostly uses parallelization of the machine process. Current high-end GPU offer higher parallelization than current high-end CPUs, due to larger number of cores. An example for this issue appears when Nvidia Tensor RT, a software development kit SDK for highly parallel machine learning, marketed to reach up to 40 × performance speed than CPU only applications. Tensor RT runs only on CUDA (compute unified device architecture), which runs only on Nvidia graphic card. Furthermore, other libraries, as "Caffe", can be used either by CPU or GPU, through switching a flag in the source code[30,31].

Localized data sets and implementations, limited to specific institutions, will cause bias in methodological validation. Thus, public records of images and datasets are preferable to decrease this bias. On the other hand, implementation doesn't suffer the same urgency for public recording[32].

While latency in offline detection could reach days, this is not acceptable in online real time detection, as the latency during endoscopy procedures will cause missing of the lesions in vivo, but improvement is more beneficial, as the ideal scenario is no latency.

While some studies showed promising results in vitro, there is still work to do offline in order to get a real time implementation which can detect neoplasia during the endoscopy conduction in vivo[33]. However, of 36 included studies in a recent meta-analysis exploring the AI integration in all types of upper GI cancers[3], only three studies were in a clinical setting and one was RCT, but even the RCT was on images not real time, and the rest of studies were on stored images offline. Furthermore, very few studies included videos or live *in vivo* validation.

The first real time study for detection of gastric cancer was performed using an online AI system with Raman spectroscopy integrated to GI endoscopy in vivo. Total computation time ranged from 100-130 milliseconds for analysis, with diagnostic accuracy of 80%[34].

Ohmori *et al*[35] introduced a new AI system that could process 36 images per second, making it adequate for RT integration in upper GI endoscopy. One concern of the authors is that limiting their processing to high quality images could impair the RT usage at the time being.

A recent meta-analysis by Arribas *et al*[3], concluded that we need to focus more on real time AI systems in upper GI endoscopy, because due to small number of studies (only two were retrieved in this metaanalysis[36,37], we are still uncertain of the feasibility of integration of AI with the endoscopists in RT situations.

In Ebigbo *et al*[37], they used a live-stream camera, examining the classification and segmentation of 14 BE patients, with diagnostic accuracy of 89.9%. AI prediction takes 1.19 s with "ensembling" and 0.13 s without "ensembling".

Luo *et al*[36] performed the first aided AI RT implementation study in upper GI endoscopy. During a case-control study in six different hospitals in China, they developed a new AI system for RT examination named Gastrointestinal Artificial

Intelligence Diagnosis System (GRAIDS), with latency of only 40 ms, and high diagnostic accuracy irrespective of the level of training of the endoscopists.

Imaging techniques, such as volumetric laser endomicroscopy, are used in BE to characterize different layers of the mucosa[38]. Characterization ideally includes the location, type and stage of neoplasia in the GI tract. A future prospect is the prognosis of this type.

"AI system is watching" is a statement that shows how endoscopists are more keen on clear videos and imaging when they know that an AI system will use those datasets [3,39].

The "blackbox" nature of CNN learning algorithms, means that we don't know how the AI system reached its diagnosis, thus no human learning could be benefited from AI neoplasia recognition[40]. This is accompanied by the lack of training and lack of learning interest in postgraduates, mostly due to the cancer prevalence problems mentioned before. The story is different in colonoscopy, where in most studies, experts in the field usually beat the AI systems or show equal diagnostic efficacy, also where experts beat beginners or junior physicians[41-44].

Another solution presented by the AI implementation, is that only one system could be used in all types of upper GI endoscopy. In a multicenter study done by Luo *et al* [36], they used a new system called GRAIDS. This system allowed for the examination of all types of upper GI neoplasms including both esophageal and gastric in a single system. In addition, the system showed similar diagnostic accuracy when compared to experts[36].

AI implementation in upper GI endoscopy proceeds first from detection (the lesion is present or not), to segmentation (the lesion is differentiated from the surrounding normal tissue), and then to characterization (the lesion is histologically predicted). A quality assessment tool for diagnostic accuracy studies called QUDAS score and its modified version are used for quality assessment of these diagnostic accuracy trials [45].

FUTURE ASPIRATIONS

One of the most promising findings was the early detection of precancerous lesions with chronic inflammatory background (chronic atrophic gastritis) with high specificity of all grades (mild, moderate and severe)[46]. This research might offer a solution to the hypothetical problem of background inflammatory state confusion with cancer. However, future validation is needed to reach our goal.

Accumulation of datasets, with the help of experts in annotating the pictures and videos of lesions in the upper GI endoscopy and linking them to the histopathological findings is mandatory for the progress of the AI in upper GI endoscopy. And public datasets will allow researchers to conduct their algorithm freely, without limitation to geographical regions or expert specialization in certain types of cancers.

Using a single system for detection of pan GI neoplasms with acceptable diagnostic accuracy for all GI regions is the ultimate goal, in addition to resolving the real time delay for image processing, which is still only scarcely examined in upper GI endoscopy.

CONCLUSION

Using AI integration with upper GI endoscopy could benefit trainees and general practitioners. Building a dataset library that is accessible to the researchers, with upper GI lesions apparent irrespective of the geographical area could be of great benefit to even experts in the fields with limited knowledge of the non-prevalent cancers in their area of practice.

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REFERENCES

1 **Arnold M**, Abnet CC, Neale RE, Vignat J, Giovannucci EL, McGlynn KA, Bray F. Global Burden of 5 Major Types of Gastrointestinal Cancer. *Gastroenterology* 2020; **159**: 335-349.e15 [PMID: 32247694 DOI: 10.1053/j.gastro.2020.02.068]

2 **Yu H**, Singh R, Shin SH, Ho KY. Artificial intelligence in upper GI endoscopy - current status, challenges and future promise. *J Gastroenterol Hepatol* 2021; **36**: 20-24 [PMID: 33448515 DOI: 10.1111/jgh.15354]

3 **Arribas J**, Antonelli G, Frazzoni L, Fuccio L, Ebigbo A, van der Sommen F, Ghatwary N, Palm C, Coimbra M, Renna F, Bergman JJGHM, Sharma P, Messmann H, Hassan C, Dinis-Ribeiro MJ. Standalone performance of artificial intelligence for upper GI neoplasia: a meta-analysis. *Gut* 2020 epub ahead of print [PMID: 33127833 DOI: 10.1136/gutjnl-2020-321922]

4 **Bang CS**, Lee JJ, Baik GH. Artificial Intelligence for the Prediction of Helicobacter Pylori Infection in Endoscopic Images: Systematic Review and Meta-Analysis Of Diagnostic Test Accuracy. *J Med Internet Res* 2020; **22**: e21983 [PMID: 32936088 DOI: 10.2196/21983]

5 **Lui TKL**, Tsui VWM, Leung WK. Accuracy of artificial intelligence-assisted detection of upper GI lesions: a systematic review and meta-analysis. *Gastrointest Endosc* 2020; **92**: 821-830.e9 [PMID: 32562608 DOI: 10.1016/j.gie.2020.06.034]

6 **Menon S**, Trudgill N. How commonly is upper gastrointestinal cancer missed at endoscopy? *Endosc Int Open* 2014; **2**: E46-E50 [PMID: 26135259 DOI: 10.1055/s-0034-1365524]

7 **Sekiguchi M**, Oda I. High miss rate for gastric superficial cancers at endoscopy: what is necessary for gastric cancer screening and surveillance using endoscopy? *Endosc Int Open* 2017; **5**: E727-E728 [PMID: 28791320 DOI: 10.1055/s-0043-112245]

8 **Kitamura Y**, Ito M, Matsuo T, Boda T, Oka S, Yoshihara M, Tanaka S, Chayama K. Characteristic epithelium with low-grade atypia appears on the surface of gastric cancer after successful Helicobacter pylori eradication therapy. *Helicobacter* 2014; **19**: 289-295 [PMID: 24766284 DOI: 10.1111/hel.12132]

9 **Ito M**, Tanaka S, Takata S, Oka S, Imagawa S, Ueda H, Egi Y, Kitadai Y, Yasui W, Yoshihara M, Haruma K, Chayama K. Morphological changes in human gastric tumours after eradication therapy of Helicobacter pylori in a short-term follow-up. *Aliment Pharmacol Ther* 2005; 21: 559-566 [PMID: 15740539 DOI: 10.1111/j.1365-2036.2005.02360.x]

10 **Yasuda T**, Yagi N, Omatsu T, Hayashi S, Nakahata Y, Yasuda Y, Obora A, Kojima T, Naito Y, Itoh Y. Benefits of linked color imaging for recognition of early differentiated-type gastric cancer: in comparison with indigo carmine contrast method and blue laser imaging. *Surg Endosc* 2021; **35**: 2750-2758 [PMID: 32556753 DOI: 10.1007/s00464-020-07706-1]

11 **Pawa R**, Chuttani R. Benefits and limitations of simulation in endoscopic training. *Tech Gastrointest Endosc* 2011; **13**: 191-198. [DOI: 10.1016/j.tgie.2011.06.005]

12 **Niu PH**, Zhao LL, Wu HL, Zhao DB, Chen YT. Artificial intelligence in gastric cancer: Application and future perspectives. *World J Gastroenterol* 2020; **26**: 5408-5419 [PMID: 33024393 DOI: 10.3748/wjg.v26.i36.5408]

13 **Chang M**. Artificial Intelligence for Drug Development, Precision Medicine, and Healthcare. 1st ed. Boca Raton: Chapman and Hall/CRC, 2020 [DOI: 10.1201/9780429345159]

14 **Sánchez-Montes C**, Bernal J, García-Rodríguez A, Córdova H, Fernández-Esparrach G. Review of computational methods for the detection and classification of polyps in colonoscopy imaging. *Gastroenterol Hepatol* 2020; **43**: 222-232 [PMID: 32143918 DOI: 10.1016/j.gastrohep.2019.11.004]

15 **Zhao Z**, Yin Z, Wang S, Wang J, Bai B, Qiu Z, Zhao Q. Meta-analysis: The diagnostic efficacy of chromoendoscopy for early gastric cancer and premalignant gastric lesions. *J Gastroenterol Hepatol* 2016; **31**: 1539-1545 [PMID: 26860924 DOI: 10.1111/jgh.13313]

16 **Bang CS**, Lim H, Jeong HM, Hwang SH. Use of Endoscopic Images in the Prediction of Submucosal Invasion of Gastric Neoplasms: Automated Deep Learning Model Development and Usability Study. *J Med Internet Res* 2021; **23**: e25167 [PMID: 33856356 DOI: 10.2196/25167]

17 **Wu L**, Zhou W, Wan X, Zhang J, Shen L, Hu S, Ding Q, Mu G, Yin A, Huang X, Liu J, Jiang X, Wang Z, Deng Y, Liu M, Lin R, Ling T, Li P, Wu Q, Jin P, Chen J, Yu H. A deep neural network improves endoscopic detection of early gastric cancer without blind spots. *Endoscopy* 2019; **51**: 522-531 [PMID: 30861533 DOI: 10.1055/a-0855-3532]

18 **Kitagawa Y**, Suzuki T, Nankinzan R, Ishigaki A, Furukawa K, Sugita O, Hara T, Yamaguchi T. Comparison of endoscopic visibility and miss rate for early gastric cancers after Helicobacter pylori eradication with white-light imaging versus linked color imaging. *Dig Endosc* 2020; 32: 769-777 [PMID: 31765047 DOI: 10.1111/den.13585]

19 **Fukuda H**, Miura Y, Osawa H, Takezawa T, Ino Y, Okada M, Khurelbaatar T, Lefor AK, Yamamoto H. Linked color imaging can enhance recognition of early gastric cancer by high color contrast to surrounding gastric intestinal metaplasia. *J Gastroenterol* 2019; **54**: 396-406 [PMID: 30291440 DOI: 10.1007/s00535-018-1515-6]

20 **Yang YJ**, Bang CS. Application of artificial intelligence in gastroenterology. *World J Gastroenterol* 2019; **25**: 1666-1683 [PMID: 31011253 DOI: 10.3748/wjg.v25.i14.1666]

21 **Willis BH**. Spectrum bias--why clinicians need to be cautious when applying diagnostic test studies. *Fam Pract* 2008; **25**: 390-396 [PMID: 18765409 DOI: 10.1093/fampra/cmn051]

22 **van der Laan JJH**, van der Waaij AM, Gabriëls RY, Festen EAM, Dijkstra G, Nagengast WB. Endoscopic imaging in inflammatory bowel disease: current developments and emerging strategies.

Expert Rev Gastroenterol Hepatol 2021; 15: 115-126 [PMID: 33094654 DOI: 10.1080/17474124.2021.1840352]

23 **Shinozaki S**, Osawa H, Hayashi Y, Lefor AK, Yamamoto H. Linked color imaging for the detection of early gastrointestinal neoplasms. *Therap Adv Gastroenterol* 2019; **12**: 1756284819885246 [PMID: 31700545 DOI: 10.1177/1756284819885246]

24 **Barbeiro S**, Libânio D, Castro R, Dinis-Ribeiro M, Pimentel-Nunes P. Narrow-Band Imaging: Clinical Application in Gastrointestinal Endoscopy. *GE Port J Gastroenterol* 2018; **26**: 40-53 [PMID: 30675503 DOI: 10.1159/000487470]

25 **Song EM**, Park B, Ha CA, Hwang SW, Park SH, Yang DH, Ye BD, Myung SJ, Yang SK, Kim N, Byeon JS. Endoscopic diagnosis and treatment planning for colorectal polyps using a deep-learning model. *Sci Rep* 2020; **10**: 30 [PMID: 31913337 DOI: 10.1038/s41598-019-56697-0]

26 **Mori Y**, Neumann H, Misawa M, Kudo SE, Bretthauer M. Artificial intelligence in colonoscopy - Now on the market. What's next? *J Gastroenterol Hepatol* 2021; **36**: 7-11 [PMID: 33179322 DOI: 10.1111/jgh.15339]

27 **Shin D**, Protano MA, Polydorides AD, Dawsey SM, Pierce MC, Kim MK, Schwarz RA, Quang T, Parikh N, Bhutani MS, Zhang F, Wang G, Xue L, Wang X, Xu H, Anandasabapathy S, Richards-Kortum RR. Quantitative analysis of high-resolution microendoscopic images for diagnosis of esophageal squamous cell carcinoma. *Clin Gastroenterol Hepatol* 2015; **13**: 272-279.e2 [PMID: 25066838 DOI: 10.1016/j.cgh.2014.07.030]

28 **Saurin JC**, Beneche N, Chambon C, Pioche M. Challenges and Future of Wireless Capsule Endoscopy. *Clin Endosc* 2016; **49**: 26-29 [PMID: 26855920 DOI: 10.5946/ce.2016.49.1.26]

29 **Nadler M**, Eliakim R. The role of capsule endoscopy in acute gastrointestinal bleeding. *Therap Adv Gastroenterol* 2014; **7**: 87-92 [PMID: 24587821 DOI: 10.1177/1756283X13504727]

30 **Lequan Yu**, Hao Chen, Qi Dou, Jing Qin, Pheng Ann Heng. Integrating Online and Offline Three-Dimensional Deep Learning for Automated Polyp Detection in Colonoscopy Videos. *IEEE J Biomed Health Inform* 2017; 21: 65-75 [PMID: 28114049 DOI: 10.1109/JBHI.2016.2637004]

31 **Akbari M**, Mohrekesh M, Rafiei S, Reza Soroushmehr SM, Karimi N, Samavi S, Najarian K. Classification of Informative Frames in Colonoscopy Videos Using Convolutional Neural Networks with Binarized Weights. *Annu Int Conf IEEE Eng Med Biol Soc* 2018; **2018**: 65-68 [PMID: 30440342 DOI: 10.1109/EMBC.2018.8512226]

32 **Chen PJ**, Lin MC, Lai MJ, Lin JC, Lu HH, Tseng VS. Accurate Classification of Diminutive Colorectal Polyps Using Computer-Aided Analysis. *Gastroenterology* 2018; **154**: 568-575 [PMID: 29042219 DOI: 10.1053/j.gastro.2017.10.010]

33 **Mori Y**, Kudo SE, Mohmed HEN, Misawa M, Ogata N, Itoh H, Oda M, Mori K. Artificial intelligence and upper gastrointestinal endoscopy: Current status and future perspective. *Dig Endosc* 2019; **31**: 378-388 [PMID: 30549317 DOI: 10.1111/den.13317]

34 **Duraipandian S**, Sylvest Bergholt M, Zheng W, Yu Ho K, Teh M, Guan Yeoh K, Bok Yan So J, Shabbir A, Huang Z. Real-time Raman spectroscopy for in vivo, online gastric cancer diagnosis during clinical endoscopic examination. *J Biomed Opt* 2012; **17**: 081418 [PMID: 23224179 DOI: 10.1117/1.JBO.17.8.081418]

35 **Ohmori M**, Ishihara R, Aoyama K, Nakagawa K, Iwagami H, Matsuura N, Shichijo S, Yamamoto K, Nagaike K, Nakahara M, Inoue T, Aoi K, Okada H, Tada T. Endoscopic detection and differentiation of esophageal lesions using a deep neural network. *Gastrointest Endosc* 2020; **91**: 301-309.e1 [PMID: 31585124 DOI: 10.1016/j.gie.2019.09.034]

36 **Luo H**, Xu G, Li C, He L, Luo L, Wang Z, Jing B, Deng Y, Jin Y, Li Y, Li B, Tan W, He C, Seeruttun SR, Wu Q, Huang J, Huang DW, Chen B, Lin SB, Chen QM, Yuan CM, Chen HX, Pu HY, Zhou F, He Y, Xu RH. Real-time artificial intelligence for detection of upper gastrointestinal cancer by endoscopy: a multicentre, case-control, diagnostic study. *Lancet Oncol* 2019; **20**: 1645-1654 [PMID: 31591062 DOI: 10.1016/S1470-2045(19)30637-0]

37 **Ebigbo A**, Mendel R, Probst A, Manzeneder J, Prinz F, de Souza LA Jr, Papa J, Palm C, Messmann H. Real-time use of artificial intelligence in the evaluation of cancer in Barrett's oesophagus. *Gut* 2020; **69**: 615-616 [PMID: 31541004 DOI: 10.1136/gutjnl-2019-319460]

38 **Wolfsen HC**. Volumetric Laser Endomicroscopy in Patients With Barrett Esophagus. *Gastroenterol Hepatol (N Y)* 2016; 12: 719-722 [PMID: 28035200]

39 **Bohr A**, Memarzadeh K. The rise of artificial intelligence in healthcare applications. *Artif Intell Healthcare* 2020; 25-60 [DOI: 10.1016/B978-0-12-818438-7.00002-2]

40 **Choi J**, Shin K, Jung J, Bae HJ, Kim DH, Byeon JS, Kim N. Convolutional Neural Network Technology in Endoscopic Imaging: Artificial Intelligence for Endoscopy. *Clin Endosc* 2020; **53**: 117-126 [PMID: 32252504 DOI: 10.5946/ce.2020.054]

41 **Hassan C**, Spadaccini M, Iannone A, Maselli R, Jovani M, Chandrasekar VT, Antonelli G, Yu H, Areia M, Dinis-Ribeiro M, Bhandari P, Sharma P, Rex DK, Rösch T, Wallace M, Repici A. Performance of artificial intelligence in colonoscopy for adenoma and polyp detection: a systematic review and meta-analysis. *Gastrointest Endosc* 2021; **93**: 77-85.e6 [PMID: 32598963 DOI: 10.1016/j.gie.2020.06.059]

42 **Lui TKL**, Guo CG, Leung WK. Accuracy of artificial intelligence on histology prediction and detection of colorectal polyps: a systematic review and meta-analysis. *Gastrointest Endosc* 2020; **92**: 11-22.e6 [PMID: 32119938 DOI: 10.1016/j.gie.2020.02.033]

43 **Barua I**, Vinsard DG, Jodal HC, Løberg M, Kalager M, Holme Ø, Misawa M, Bretthauer M, Mori Y. Artificial intelligence for polyp detection during colonoscopy: a systematic review and meta-analysis.

Endoscopy 2021; **53**: 277-284 [PMID: 32557490 DOI: 10.1055/a-1201-7165]

44 **Aziz M**, Fatima R, Dong C, Lee-Smith W, Nawras A. The impact of deep convolutional neural network-based artificial intelligence on colonoscopy outcomes: A systematic review with meta-analysis. *J Gastroenterol Hepatol* 2020; **35**: 1676-1683 [PMID: 32267558 DOI: 10.1111/jgh.15070]

45 **Whiting PF**, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MM, Sterne JA, Bossuyt PM; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; **155**: 529-536 [PMID: 22007046 DOI: 10.7326/0003-4819-155-8-201110180-00009]

46 **Zhang Y**, Li F, Yuan F, Zhang K, Huo L, Dong Z, Lang Y, Zhang Y, Wang M, Gao Z, Qin Z, Shen L. Diagnosing chronic atrophic gastritis by gastroscopy using artificial intelligence. *Dig Liver Dis* 2020; **52**: 566-572 [PMID: 32061504 DOI: 10.1016/j.dld.2019.12.146]

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MINIREVIEWS

Application of artificial intelligence in liver diseases: From diagnosis to treatment

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Abstract

Infectious or noninfectious liver disease has inexorably risen as one of the leading causes of global death and disease burden. There were an estimated 2.14 million liver-related deaths in 2017, representing an 11.4% increase since 2012. Traditional diagnosis and treatment methods have various dilemmas in different causes of liver disease. As a hot research topic in recent years, the application of artificial intelligence (AI) in different fields has attracted extensive attention, and new technologies have brought more ideas for the diagnosis and treatment of some liver diseases. Machine learning (ML) is the core of AI and the basic way to make a computer intelligent. ML technology has many potential uses in hepatology, ranging from exploring new noninvasive means to predict or diagnose different liver diseases to automated image analysis. The application of ML in liver diseases can help clinical staff to diagnose and treat different liver diseases quickly, accurately and scientifically, which is of importance for reducing the incidence and mortality of liver diseases, reducing medical errors, and promoting the development of medicine. This paper reviews the application and prospects of AI in liver diseases, and aims to improve clinicians' awareness of the importance of AI in the diagnosis and treatment of liver diseases.

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Core tip: Liver disease has inexorably risen as one of the leading causes of global death and disease burden. As a hot research topic in recent years, the application of artificial intelligence (AI) in medical fields has attracted extensive attention. The application of machine learning in the liver diseases can help clinical staff to diagnose and treat different liver diseases quickly, accurately and scientifically, which is of importance for reducing the incidence and mortality of liver diseases, reducing medical errors, and promoting the development of medicine. This paper reviews the application and prospects of AI in liver diseases.

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INTRODUCTION

Infectious or noninfectious liver diseases cause a significant disease burden. There were an estimated 2.14 million liver-related deaths in 2017, representing an 11.4% increase since 2012[1]. Traditional diagnosis and treatment methods have various dilemmas in different causes of liver disease. With the development of artificial intelligence (AI) technology, new technologies have brought more ideas for the diagnosis and treatment of some liver diseases.

AI is an algorithm-based application field that simulates human mental processes and intellectual activities, enabling machines to solve problems with knowledge. In the information age, AI is widely used in the medical field and can provide accurate diagnosis and treatment for complex diseases, reduce medical errors, and promote the development of medicine[2]. For example, using deep learning architecture visual pattern analysis to detect basal cell carcinoma and distinguish malignant and benign lesions, the diagnosis accuracy rate is > 90% compared with experts[3]. There are two common types of AI. The first type is expert systems and the second is machine learning (ML), which is the core of AI and the basic way to make a computer intelligent (Figure 1). ML requires many data to train, which systematically improves computer performance in the process. By doing so, computers are able to shed light on previously unascertainable relationships that traditional statistical methods could not detect. ML is also capable of analyzing data types that were previously unavailable for advanced computer analysis, such as image and text data.

The area offering the most exciting new applications in healthcare is ML. Many studies in recent years have suggested that ML technology has many potential uses in hepatology, ranging from exploring new noninvasive means to predict or diagnose different liver diseases to automated image analysis. From the identification of liver areas at risk of radiation toxicity to the use of drug structures to predict the risk of liver injury, the accuracy of diagnosis and the effectiveness of treatment can be improved, and the efficiency can also be improved through automation. Although promising data from preclinical studies are now available, the application of AI in liver disease is far from being applied in clinical practice, so the application of AI in liver disease and other diseases remains challenging and deserves further study.

NEW ROUTES OF LIVER DISEASE DIAGNOSIS

Liver disease is not an independent disease. Because the specific types of lesions are different, the diagnostic methods differ. Different examination methods can be selected according to the specific types of liver diseases to be examined. For example, at present, the common diagnostic method for nonalcoholic fatty liver disease (NAFLD) is liver ultrasound (US)[4,5]; the common diagnostic method for liver fibrosis is liver biopsy[4]; the diagnosis of liver cancer (LC) mainly uses imaging images and biomarkers, and the staging mainly uses the Barcelona staging system. However, due to subjective and invasive factors, the current examination methods have certain limitations in the diagnosis of some liver diseases. The sensitivity and

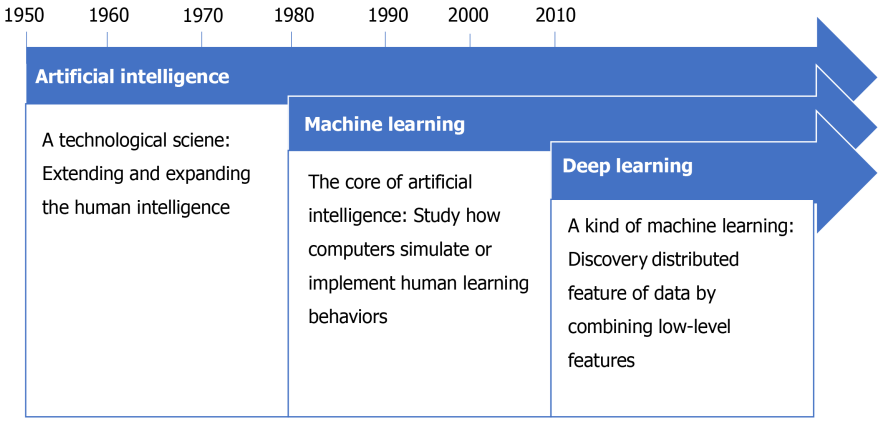

Figure 1 Timeline of the main concepts of artificial intelligence.

specificity of liver US decrease with increasing body mass index because US is subjective. As a solid tumor, hepatocellular carcinoma (HCC) has significant temporal and spatial heterogeneity, which can predict the treatment response and prognosis of HCC[6]. The Barcelona staging system does not include the histological and molecular characteristics of tumors. The application of AI has filled the gaps in these respects. By designing noninvasive examination means to intelligently analyze images and pictures, AI has improved the diagnostic efficiency and accuracy of clinicians.

Design noninvasive examination

The prevalence of NAFLD is currently increasing, and there are currently no accurate diagnostic means or targeted medicines. The application of AI can realize the early diagnosis of NAFLD, which is expected to reduce the further deterioration of the disease. Current research has developed automatic liver segmentation based on deep learning tools used for quantitative abdominal computed tomography (CT) of liver fat. This fully automated CT tool provides rapid and objective assessment that can be used in a large retrospective cohort for future studies. If hepatic steatosis proves to be an independent risk factor for future adverse events, the automated tool can also be used for opportunistic NAFLD screening with any nonenhanced CT, including liver (abdomen or chest) scan, regardless of the clinical indications of imaging[7]. In addition, a technique that combines noninvasive markers with the ML approach is suitable for optimal identification of NAFLD risk assessment and can also be extended to predict other types of disease caused by metabolic syndrome[8]. The use of ML algorithms to establish a prediction model of NAFLD based on laboratory parameters is also a current research direction. A prediction model named the NAFLD ridge score, which can be easily calculated and obtain a high negative predictive value, is recommended as the simplest and most predictive ML model to exclude NAFLD[9].

Liver fibrosis, regardless of the etiology, is believed to be key to the progression of any form of chronic liver disease (CLD), and persistent fibrosis is widely believed to be a major driver of the eventual development of cirrhosis and liver failure[10,11]. Liver biopsy is considered to be the gold standard for staging liver fibrosis; however, it is invasive and is limited by sample error, interobserver variability and various potential complications[12]. Radiological and serum markers of fibrosis are also used to assess liver fibrosis[13], and it is not reliable to accurately distinguish the stages of fibrosis in these patterns. There is a clear need for safe, effective and reliable noninvasive assessment modalities. A study that aimed to develop and validate a deep learning system (DLS) for staging liver fibrosis by using portal venous phase CT images demonstrated that a DLS trained by using a large amount of CT data allowed for highly accurate staging of liver fibrosis. In this study, DLS was superior to radiologists and serum fibrosis tests in diagnosing significant fibrosis, advanced fibrosis and cirrhosis[14]. In addition, an existing model called deep learning radiomics of elastography has shown the best overall performance in predicting liver fibrosis stage, which has certain value and practical value for the accurate noninvasive diagnosis of liver fibrosis stage in hepatitis-B-virus-infected patients[15].

Dig deeper into the medical images

HCC is the most common primary liver cancer and has significant temporal and spatial heterogeneity. AI-based imaging, i.e., imaging omics, can quantitatively

analyze tumor imaging to reveal the imaging manifestations of these heterogeneous characteristics. The concept of imaging omics was first proposed by Lambin *et al*[16] in 2012. It mainly extracts a large number of influential features from high-throughput radiological images and then uses statistics and AI algorithms to select the most valuable imaging omics to construct tumor predictive models. In essence, the significance of imaging omics is to dig deeper into the information of traditional medical images to compensate for the deficiency of the human eye.

Similarly, there is a need for better clinical classification of indeterminate liver nodules; however, the use of a single biomarker to predict the presence of cancer is difficult due to its multifactorial nature[17]. An AI-based predictive model of HCC reduced the misclassification rate by approximately half compared with that of a single tumor marker[18]. In addition, radiomics ML can be trained to diagnose hepatic nodules using the European Association for the Study of the Liver (EASL) guidelines in patients with HCC disease classified as uncertain cirrhosis[19]. According to EASL, indeterminate nodules include all nodules that do not provide arterial enhancement and washout [two major Liver Imaging Reporting and Data System (LI-RADS) features] and require biopsy regardless of LI-RADS; however, biopsies of cirrhosis carry life-threatening risks, including bleeding and tumor spread[20]. A study demonstrated that ML-based radiometric features using arterial and portal phase quantitative CT feature changes can enable the noninvasive diagnosis of HCC in patients with indeterminate nodules of cirrhosis. This feature will help to identify patients at high risk of HCC who should be prioritized for treatment to achieve significant clinical benefits[19].

AN ALTERNATIVE TREATMENT OPTION FOR LIVER DISEASES

Worldwide, CLD is a leading cause of morbidity and mortality[21]. There are a few therapeutic approaches for liver dysfunction, such as direct antiviral drugs (DAAs) for hepatitis C virus (HCV) and transarterial chemoembolization (TACE) for HCC[22]. Because some patients are resistant to DAAs and do not respond well to antiviral therapy and individualized responses to primary TACE vary among patients, AI seems to be an alternative option. AI has attracted attention for treatment of liver diseases in recent years, especially hepatitis C and LC[23]. AI can go beyond human reasoning to build drug-resistance predictive models from many complex combinations and overcome the limitations of traditional techniques, which may be effective in avoiding the emergence of a resistant virus, reducing medical costs and providing precise and personalized treatment advice for doctors and patients.

Build predictive models

With the popularization of DAAs and the application of new detection technologies and service models, global progress has been made in the detection and treatment of HCV. However, some patients with HCV are resistant to DAAs and do not respond well to antiviral therapy, and the current lack of means to screen these patients may delay disease treatment. AI algorithms can go beyond human reasoning to build predictive models from many complex combinations. A current study identified all variants of HCV whole-genome sequences that could be evaluated, and a support vector machine (SVM) based on a machine algorithm was the best prediction model. Similar models can be used to determine the best treatment for other viral infections and cancers[24].

Coinfection with human immunodeficiency virus 1 and HCV is common in some populations today; however, treating coinfections is a challenge. A previous study demonstrated that a multiple quantitative structure–activity relationship model showed high performance in predicting multitarget inhibitors with anti-HIV and -HCV activity[25]. The application of ML methods enables us to identify variables associated with reduced HCV treatment intake. The most recent variable, people who inject drugs (PWIDs), was identified as a major limiting factor associated with therapeutic intake deficit, even when priority criteria were met. PWIDs refers to people who have been injected at some point but are not currently using oral contraceptives or abusing drugs. In fact, intelligent network interruption analysis has been used as a targeted strategy to effectively interrupt HCV transmission between PWIDs [26]. Its application in clinical decision-making of infectious diseases should be expanded to optimize treatment and prevention strategies.

Provide personalized treatment advice

Due to the well-known limitations of TACE, AI seems to be an alternative treatment option for HCC. Some studies have reported the use of fusion imaging (FI) techniques to overcome the limitations of traditional techniques. FI is an AI-based technology that allows the fusion of two different imaging modes[27]. A prospective randomized study conducted by Huang *et al*[28] showed that the technical response rate of FI in ablation for hepatic nodules < 5 cm was close to 100% and reported the special usefulness of FI in tumors at less obvious and dangerous sites, not only to accurately delineate the target lesion and critical organs, the structures that may be close to the target area of ablation can also be accurately delineated.

The clinical decision support system (CDSS) is the software that is designed to be a direct aid to clinical decision-making, in which the characteristics of an individual patient are matched to a computerized clinical knowledge base and patient-specific assessments or recommendations are then presented to the clinician or the patient for a decision[29]. One study applied AI technology to clinical realworld data of patients with primary HCC, explored the precise treatment of disease and built up the AIbased CDSS, HCC CDSS. In the internal use verification process of HCC CDSS in West China Hospital, the matching accuracy rate between HCC CDSS and the multidisciplinary team treatment scheme reached 95.10%. This scheme is conducive to optimizing the clinical treatment decision of LC and can provide precise and personalized treatment advice for doctors and patients[30].

AI-DRIVEN PREDICTION FOR LIVER INJURY

Drug-induced liver injury (DILI) is a serious problem in clinical treatment and a common cause of drug development failure or withdrawal from the market[31]. Therefore, compound hepatotoxicity is important to determine.

Accurate estimation of the prognosis of patients with liver disease can help clinicians make appropriate treatment plans for different individuals; however, due to the complex process of CLD, the extensive impact on the systemic system and organs, and the lack of an adequate understanding of the nature of the development of liver disease, the understanding of the prognosis of different liver diseases is still limited. In recent years, HCV infection among LC patients and the mortality rate of HCV have been on the rise. Therefore, prediction of the prognosis of HCV patients has also attracted attention. Cirrhosis is a common, high-risk disease with slow clinical progression, and readmission and death in patients with cirrhosis are common and unpredictable. None of the clinically available predictive scores for cirrhosis can account for the broad range of clinical and psychosocial factors that may be associated with cirrhosis mortality. Individualized responses to primary TACE vary among patients with HCC. In addition, identifying a robust survival subgroup for HCC would also significantly improve patient care. The application of the prediction model of disease prognosis based on AI can improve the understanding of the prognosis of some liver diseases to a certain extent and provide an auxiliary reference for doctors' decision-making.

Analyze drug structure

AI is a low-cost, fast method to collect information on potential toxicity, and great efforts have been made in hepatotoxicity prediction in recent years. A study proposed that the integration of the Top-5 model could significantly improve the performance of hepatotoxicity prediction. The integrated Top-5 model consists of five base classifiers: Random Forest (RF) using Substructure Count, SVM using Chemistry Development Kit Extended, SVM using Chemistry Development Kit, SVM using PubChem, and RF using Klekota–Roth Count[32]. The deep learning model is also a stable and highly accurate predictive model of DILI, which can provide very useful safety information for early drug discovery and rational clinical drug use[33].

Predict risk of deterioration and mortality

The prediction of the prognosis of HCV patients has attracted attention in recent years. One study showed that the recurrent neural network model was superior to the logistic regression (LR) model in predicting HCC risk in patients with HCV-associated cirrhosis, including patients with supraventricular tachycardia following antiviral therapy; thus, it can be used to identify patients at high risk for HCV-associated cirrhosis to develop HCC and to inform risk-based HCC expansion and surveillance strategies[34].

None of the clinically available predictive scores for cirrhosis can account for the broad range of clinical and psychosocial factors that may be associated with cirrhosis mortality. ML techniques have been used to help fill these gaps in cirrhosis but are not yet widely available. In one study, three AI models were established, including LR, kernel SVM and RF classifier, and showed that these models had difficulty predicting readmissions and deaths in cirrhosis at 30 and 90 d. The accuracy of the AI model is comparable to that generated using the model for the end-stage liver disease-NA (MELD-NA) score alone, requiring additional biomarkers to improve the predictive power[35].

Another study developed and validated a cirrhosis mortality model (CIMM) using variables selected from ML algorithms. The results showed that ML can help select important variables for more transparent risk scoring while maintaining high accuracy. The synthetic hybrid CIMM performed better than the widely used model for MELD-NA score[36].

Speculate personalized response

For patients with LC, individualized responses to primary TACE vary. An AI-based radiomics strategy quantitatively analyses contrast-enhanced US images to predict personalized responses to primary TACE in HCC. There is potential for better selection of Barcelona Clinical Liver Cancer stage B patients receiving hepatic TACE and for better optimization of treatment planning and follow-up monitoring in the HCC management process[37].

Identifying a robust survival subgroup for HCC would also significantly improve patient care. Currently, few studies have integrated multiomics data to definitively predict HCC survival in a multipatient cohort. The survival-sensitive subtype model-deep learning model is of importance for the prognostic prediction and treatment intervention of HCC[38].

CONCLUSION

AI has become an important part of liver disease research, improving diagnostic accuracy, improving decision-making by enhancing predictive power, increasing efficiency through automation, and even predicting liver disease prognosis. Analysis of key biomarkers using ML can also provide deeper insights into the pathophysiology of liver disease. Despite the challenges, the application of AI in the field of liver disease is promising and worthy of further study. Researchers need to further develop new models of AI in liver disease diagnosis and precise treatment and conduct clinical verification to improve the accuracy of the results and promote the clinical application of AI. However, we must also be wary of over-reliance on such algorithms. AI will support rather than replace doctors, although computers and healthcare workers will have to work together. Ultimately, healthcare workers will have to make decisions for their patients based on their preferences, circumstances and ethics.

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REFERENCES

1 **Paik JM**, Golabi P, Younossi Y, Mishra A, Younossi ZM. Changes in the Global Burden of Chronic Liver Diseases From 2012 to 2017: The Growing Impact of NAFLD. *Hepatology* 2020; **72**: 1605-1616 [PMID: 32043613 DOI: 10.1002/hep.31173]

2 **Miller DD**, Brown EW. Artificial Intelligence in Medical Practice: The Question to the Answer? *Am J Med* 2018; **131**: 129-133 [PMID: 29126825 DOI: 10.1016/j.amjmed.2017.10.035]

3 **Mori K**, Sakuma I, Sato Y, Barillot C, Navab N. Preface. The 16th International Conference on Medical Image Computing and Computer Assisted Intervention, MICCAI 2013 was held in Nagoya, Japan during September 22-26, 2013. *Med Image Comput Comput Assist Interv* 2013; **16**: V-X [PMID: 24579116]

4 **Chalasani N**, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, Harrison SA, Brunt EM, Sanyal AJ. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. *Hepatology* 2018; **67**: 328-357 [PMID:

28714183 DOI: 10.1002/hep.29367]
5 **Mancini M**, Summers P, Faita F, Brunetto MR, Callea F, De Nicola A, Di Lascio N, Farinati F, Gastaldelli A, Gridelli B, Mirabelli P, Neri E, Salvadori PA, Rebelos E, Tiribelli C, Valenti L, Salvatore M, Bonino F. Digital liver biopsy: Bio-imaging of fatty liver for translational and clinical research. *World J Hepatol* 2018; **10**: 231-245 [PMID: 29527259 DOI: 10.4254/wjh.v10.i2.231]
6 **Lewis S**, Hectors S, Taouli B. Radiomics of hepatocellular carcinoma. *Abdom Radiol (NY)* 2021; **46**: 111-123 [PMID: 31925492 DOI: 10.1007/s00261-019-02378-5]
7 **Graffy PM**, Sandfort V, Summers RM, Pickhardt PJ. Automated Liver Fat Quantification at Nonenhanced Abdominal CT for Population-based Steatosis Assessment. *Radiology* 2019; **293**: 334-342 [PMID: 31526254 DOI: 10.1148/radiol.2019190512]
8 **Perveen S**, Shahbaz M, Keshavjee K, Guergachi A. A Systematic Machine Learning Based Approach for the Diagnosis of Non-Alcoholic Fatty Liver Disease Risk and Progression. *Sci Rep* 2018; **8**: 2112 [PMID: 29391513 DOI: 10.1038/s41598-018-20166-x]
9 **Yip TC**, Ma AJ, Wong VW, Tse YK, Chan HL, Yuen PC, Wong GL. Laboratory parameter-based machine learning model for excluding non-alcoholic fatty liver disease (NAFLD) in the general population. *Aliment Pharmacol Ther* 2017; **46**: 447-456 [PMID: 28585725 DOI: 10.1111/apt.14172]
10 **Dranoff JA**, Wells RG. Portal fibroblasts: Underappreciated mediators of biliary fibrosis. *Hepatology* 2010; **51**: 1438-1444 [PMID: 20209607 DOI: 10.1002/hep.23405]
11 **Rosselli M**, MacNaughtan J, Jalan R, Pinzani M. Beyond scoring: a modern interpretation of disease progression in chronic liver disease. *Gut* 2013; **62**: 1234-1241 [PMID: 23645629 DOI: 10.1136/gutjnl-2012-302826]
12 **Standish RA**, Cholongitas E, Dhillon A, Burroughs AK, Dhillon AP. An appraisal of the histopathological assessment of liver fibrosis. *Gut* 2006; **55**: 569-578 [PMID: 16531536 DOI: 10.1136/gut.2005.084475]
13 **Masuzaki R**, Kanda T, Sasaki R, Matsumoto N, Ogawa M, Matsuoka S, Karp SJ, Moriyama M. Noninvasive Assessment of Liver Fibrosis: Current and Future Clinical and Molecular Perspectives. *Int J Mol Sci* 2020; **21**: 4906 [PMID: 32664553 DOI: 10.3390/ijms21144906]
14 **Choi KJ**, Jang JK, Lee SS, Sung YS, Shim WH, Kim HS, Yun J, Choi JY, Lee Y, Kang BK, Kim JH, Kim SY, Yu ES. Development and Validation of a Deep Learning System for Staging Liver Fibrosis by Using Contrast Agent-enhanced CT Images in the Liver. *Radiology* 2018; **289**: 688-697 [PMID: 30179104 DOI: 10.1148/radiol.2018180763]
15 **Wang K**, Lu X, Zhou H, Gao Y, Zheng J, Tong M, Wu C, Liu C, Huang L, Jiang T, Meng F, Lu Y, Ai H, Xie XY, Yin LP, Liang P, Tian J, Zheng R. Deep learning Radiomics of shear wave elastography significantly improved diagnostic performance for assessing liver fibrosis in chronic hepatitis B: a prospective multicentre study. *Gut* 2019; **68**: 729-741 [PMID: 29730602 DOI: 10.1136/gutjnl-2018-316204]
16 **Lambin P**, Rios-Velazquez E, Leijenaar R, Carvalho S, van Stiphout RG, Granton P, Zegers CM, Gillies R, Boellard R, Dekker A, Aerts HJ. Radiomics: extracting more information from medical images using advanced feature analysis. *Eur J Cancer* 2012; **48**: 441-446 [PMID: 22257792 DOI: 10.1016/j.ejca.2011.11.036]
17 **Sanyal AJ**, Yoon SK, Lencioni R. The etiology of hepatocellular carcinoma and consequences for treatment. *Oncologist* 2010; **15** Suppl 4: 14-22 [PMID: 21115577 DOI: 10.1634/theoncologist.2010-S4-14]
18 **Sato M**, Morimoto K, Kajihara S, Tateishi R, Shiina S, Koike K, Yatomi Y. Machine-learning Approach for the Development of a Novel Predictive Model for the Diagnosis of Hepatocellular Carcinoma. *Sci Rep* 2019; **9**: 7704 [PMID: 31147560 DOI: 10.1038/s41598-019-44022-8]
19 **Mokrane FZ**, Lu L, Vavasseur A, Otal P, Peron JM, Luk L, Yang H, Ammari S, Saenger Y, Rousseau H, Zhao B, Schwartz LH, Dercle L. Radiomics machine-learning signature for diagnosis of hepatocellular carcinoma in cirrhotic patients with indeterminate liver nodules. *Eur Radiol* 2020; **30**: 558-570 [PMID: 31444598 DOI: 10.1007/s00330-019-06347-w]
20 **European Association for the Study of the Liver**. EASL Clinical Practice Guidelines: Management of hepatocellular carcinoma. *J Hepatol* 2018; **69**: 182-236 [PMID: 29628281 DOI: 10.1016/j.jhep.2018.03.019]
21 **Asrani SK**, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. *J Hepatol* 2019; **70**: 151-171 [PMID: 30266282 DOI: 10.1016/j.jhep.2018.09.014]
22 **Park JW**, Chen M, Colombo M, Roberts LR, Schwartz M, Chen PJ, Kudo M, Johnson P, Wagner S, Orsini LS, Sherman M. Global patterns of hepatocellular carcinoma management from diagnosis to death: the BRIDGE Study. *Liver Int* 2015; **35**: 2155-2166 [PMID: 25752327 DOI: 10.1111/liv.12818]
23 **Spann A**, Yasodhara A, Kang J, Watt K, Wang B, Goldenberg A, Bhat M. Applying Machine Learning in Liver Disease and Transplantation: A Comprehensive Review. *Hepatology* 2020; **71**: 1093-1105 [PMID: 31907954 DOI: 10.1002/hep.31103]
24 **Haga H**, Sato H, Koseki A, Saito T, Okumoto K, Hoshikawa K, Katsumi T, Mizuno K, Nishina T, Ueno Y. A machine learning-based treatment prediction model using whole genome variants of hepatitis C virus. *PLoS One* 2020; **15**: e0242028 [PMID: 33152046 DOI: 10.1371/journal.pone.0242028]
25 **Wei Y**, Li W, Du T, Hong Z, Lin J. Targeting HIV/HCV Coinfection Using a Machine Learning-Based Multiple Quantitative Structure-Activity Relationships (Multiple QSAR) Method. *Int J Mol Sci* 2019; **20**: 3572 [PMID: 31336592 DOI: 10.3390/ijms20143572]

26 **Rivero-Juárez A**, Guijo-Rubio D, Tellez F, Palacios R, Merino D, Macías J, Fernández JC, Gutiérrez PA, Rivero A, Hervás-Martínez C. Using machine learning methods to determine a typology of patients with HIV-HCV infection to be treated with antivirals. *PLoS One* 2020; **15**: e0227188 [PMID: 31923277 DOI: 10.1371/journal.pone.0227188]

27 **Abi-Jaoudeh N**, Kruecker J, Kadoury S, Kobeiter H, Venkatesan AM, Levy E, Wood BJ. Multimodality image fusion-guided procedures: technique, accuracy, and applications. *Cardiovasc Intervent Radiol* 2012; **35**: 986-998 [PMID: 22851166 DOI: 10.1007/s00270-012-0446-5]

28 **Huang Q**, Zeng Q, Long Y, Tan L, Zheng R, Xu E, Li K. Fusion imaging techniques and contrast-enhanced ultrasound for thermal ablation of hepatocellular carcinoma - A prospective randomized controlled trial. *Int J Hyperthermia* 2019; **36**: 1207-1215 [PMID: 31813295 DOI: 10.1080/02656736.2019.1687945]

29 **Sim I**, Gorman P, Greenes RA, Haynes RB, Kaplan B, Lehmann H, Tang PC. Clinical decision support systems for the practice of evidence-based medicine. *J Am Med Inform Assoc* 2001; **8**: 527-534 [PMID: 11687560 DOI: 10.1136/jamia.2001.0080527]

30 **Yang J**, Guo F, Lyu T, Yan LN, Wen TF, Yang JY, Wu H, Wang WT, Song JL, Xu H, Zhang QH. Research of artificial intelligence-based clinical decision support system for primary hepatocellular carcinoma. *Zhonghua Yi Xue Za Zhi* 2020; **100**: 3870-3873 [PMID: 33371633 DOI: 10.3760/cma.j.cn112137-20200905-02571]

31 **Segall MD**, Barber C. Addressing toxicity risk when designing and selecting compounds in early drug discovery. *Drug Discov Today* 2014; **19**: 688-693 [PMID: 24451294 DOI: 10.1016/j.drudis.2014.01.006]

32 **Ai H**, Chen W, Zhang L, Huang L, Yin Z, Hu H, Zhao Q, Zhao J, Liu H. Predicting Drug-Induced Liver Injury Using Ensemble Learning Methods and Molecular Fingerprints. *Toxicol Sci* 2018; **165**: 100-107 [PMID: 29788510 DOI: 10.1093/toxsci/kfy121]

33 **Feng C**, Chen H, Yuan X, Sun M, Chu K, Liu H, Rui M. Gene Expression Data Based Deep Learning Model for Accurate Prediction of Drug-Induced Liver Injury in Advance. *J Chem Inf Model* 2019; **59**: 3240-3250 [PMID: 31188585 DOI: 10.1021/acs.jcim.9b00143]

34 **Ioannou GN**, Tang W, Beste LA, Tincopa MA, Su GL, Van T, Tapper EB, Singal AG, Zhu J, Waljee AK. Assessment of a Deep Learning Model to Predict Hepatocellular Carcinoma in Patients With Hepatitis C Cirrhosis. *JAMA Netw Open* 2020; **3**: e2015626 [PMID: 32870314 DOI: 10.1001/jamanetworkopen.2020.15626]

35 **Hu C**, Anjur V, Saboo K, Reddy KR, O'Leary J, Tandon P, Wong F, Garcia-Tsao G, Kamath PS, Lai JC, Biggins SW, Fallon MB, Thuluvath P, Subramanian RM, Maliakkal B, Vargas H, Thacker LR, Iyer RK, Bajaj JS. Low Predictability of Readmissions and Death Using Machine Learning in Cirrhosis. *Am J Gastroenterol* 2021; **116**: 336-346 [PMID: 33038139 DOI: 10.14309/ajg.0000000000000971]

36 **Kanwal F**, Taylor TJ, Kramer JR, Cao Y, Smith D, Gifford AL, El-Serag HB, Naik AD, Asch SM. Development, Validation, and Evaluation of a Simple Machine Learning Model to Predict Cirrhosis Mortality. *JAMA Netw Open* 2020; **3**: e2023780 [PMID: 33141161 DOI: 10.1001/jamanetworkopen.2020.23780]

37 **Liu D**, Liu F, Xie X, Su L, Liu M, Kuang M, Huang G, Wang Y, Zhou H, Wang K, Lin M, Tian J. Accurate prediction of responses to transarterial chemoembolization for patients with hepatocellular carcinoma by using artificial intelligence in contrast-enhanced ultrasound. *Eur Radiol* 2020; **30**: 2365-2376 [PMID: 31900703 DOI: 10.1007/s00330-019-06553-6]

38 **Chaudhary K**, Poirion OB, Lu L, Garmire LX. Deep Learning-Based Multi-Omics Integration Robustly Predicts Survival in Liver Cancer. *Clin Cancer Res* 2018; **24**: 1248-1259 [PMID: 28982688 DOI: 10.1158/1078-0432.CCR-17-0853]

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