International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 8, No. 1, 2024

Research Progress of Deep Learning in Diagnosis, Treatment and Prognosis Assessment of Hepatocellular Carcinoma

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Abstract: Hepatic carcinoma (HCC) is a common malignant tumor in the abdominal system in China. Due to its high degree of malignancy, poor prognosis and easy recurrence, there are many therapeutic programs available, but the results are not satisfactory. The use of deep learning (DL) for diagnosis, treatment and prognosis assessment of HCC patients has become a hot topic at present. Therefore, this paper reviews the application of DL in early diagnosis, microvascular infiltration, pathological grading and postoperative evaluation of HCC.

Keywords: Hepatocellular Carcinoma; Deep Learning; Convolutional Beutral Network; Microvascular Invasion; Transhepatic Arterial Chem Otherapy and Embolization.

1. Introduction

Hepatocellular carcinoma (HCC) is a common malignant tumor in the digestive system in our country. HCC is highly malignant with poor prognosis, and patients are often in the advanced stage when diagnosed, leading to a lower five-year survival rate for HCC patients. Studies have shown that the survival rate of early-stage HCC patients treated in time is much higher than that of late-stage HCC patients[1, 2]. Image analysis is susceptible to subjective factors, and when HCC lacks typical characteristics, it poses certain difficulties for early diagnosis. Deep learning (DL) is a collective term for a class of neural network algorithms, belonging to the field of machine learning computer vision[3], Convolutional neural networks (CNN) are one of the classic DL models, consisting of input layers, convolutional layers, pooling layers, fully connected layers, and output layers[4]. DL in the field of medical imaging can assist clinicians in early diagnosis and treatment, pathological grading, and prognosis assessment of HCC patients, bringing new hope for improving patient prognosis.

2. DL in HCC Diagnosis and Treatment

2.1. DL for HCC Lesion Segmentation and Early Predictive Diagnosis

Tumor volume segmentation is an emerging field in radiomics, extracting a large number of features from high-throughput data that reflect fundamental tissue biological information. Accurate measurement of tumor volume before surgery helps clinicians choose treatment plans and assess responses, so more and more scholars are trying to apply deep learning (DL) to automatic or semi-automatic segmentation of HCC images in HCC, and have made substantial progress. Said[5]used a CNN model for semi-automatic segmentation of HCC tumors on MRI, and the results showed that the semi-automatic model with manual correction improved efficiency without changing the consistency of volume measurement. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) has the characteristic of multi-phase imaging, and some scholars[6]proposed a two-stage progressive attention diagnostic framework for automatic segmentation of HCC on DCE-MRI. This framework can effectively capture key features from multi-phase images while reducing redundant noise, thereby improving model accuracy. Luo[7]built a DL model by integrating multi-stage DCE-MRI image information and 3D U-net architecture, using steps such as phase registration, pre-trained model automatic extraction of liver area, multi-stage DL model automatic segmentation of HCC lesions, integrated five-fold prediction, and using connected component analysis to achieve automatic segmentation of HCC lesions. Another scholar[8]established a four-dimensional DL model based on three-dimensional convolution and convolutional long short-term memory, using DCE-MRI image information to assist in the segmentation of HCC lesions. They mapped and analyzed the extracted features, visualizing the learning process of the proposed network model. The dynamic network biomarker theory can reflect the connections between disease gene networks through a small amount of sample data. By combining with image convolutional neural networks to build a joint model, it can cluster the key states of HCC progression, thereby reducing the filtration of effective information, which has great potential for early prediction and diagnosis of HCC[9]. Okimoto[10]found through research and comparison of DL reconstruction algorithms and traditional hybrid iterative reconstruction algorithms in CT detection of HCC that the DL reconstruction algorithm has higher detection sensitivity for small liver cancer than previous research results, which may be attributed to the optimization and improvement of the main features of HCC during the operation process. In addition, by introducing compressed sensing technology, it can effectively solve the problems of low signal-to-noise ratio, low spatial resolution, and a large amount of distortion in phase encoding artifacts in DWI imaging, while improving the detection ability of HCC[11].

2.2. Predicting Microvascular Invasion in HCC Using DL Algorithms

Microvascular invasion (MVI) refers to the presence of cancer cell nests within the vascular endothelium under a microscope, which is considered an independent risk factor for early recurrence and low survival rates in hepatocellular carcinoma (HCC). Accurate preoperative prediction of MVI is of great significance for the selection of treatment plans and prognosis assessment in HCC patients[12].Automatic segmentation errors due to deep learning (DL) can easily lead to inaccurate lesion edge localization and loss of effective features, thereby reducing the accuracy of MVI prediction. Adopting tumor expansion methods has improved this issue to some extent. A study[13]found that the 6mm area surrounding the tumor performed best in terms of AUC, accuracy, and specificity after a series of comparative trials. In recent years, several studies have confirmed[14, 15]the effectiveness of monomodal radiomics models built using CT or MRI image data for predicting MVI. However, CT and MRI scanning methods are complementary in many aspects, and the construction of multimodal DL models using both CT and MRI data is still rare. Lei[16]successfully predicted MVI based on multimodal DL models built from CT and MRI image data. Although multimodal DL models have the advantages of being efficient and simple, the lack of integration and guidance of medical expertise in the process makes the overall experimental process lack interpretability, which to some extent hinders their clinical application. Currently, two methods are commonly used to improve interpretability: embedding clinical knowledge during training or explaining DL models after training. Several scholars[17]proposed a two-stage expert-guided diagnostic framework and applied it to MVI prediction analysis. The study used interpretable features to guide the training of the diagnostic network, and the results showed that the framework has the role of interpretability and improving diagnostic accuracy. Image convolutional network models are a DL method applied to image and node classification, and they also have great potential in interpretability. By learning attributes and structures end-to-end, the results are interpretable[18]. Liu[19]designed a learnable online class activation map in the experiment, drawing on the pathological diagnostic process to guide, enabling the DL network to accurately locate the high-incidence areas of MVI, fully explore the representation of MVI, thereby improving the model's interpretability and stability. Different from previous studies predicting HCC MVI based on MRI semantic features, some scholars[20]extracted survival environmental analysis related to HCC invasiveness and DL features, and built a fusion model combining these two types of features. The study also added class activation maps to make features interpretable, and the results showed that the fusion model has potential.

2.3. The Application of DL in the Typing and Grading of HCC Histopathology

Histopathological analysis helps in clinically distinguishing benign and malignant lesions and is the gold standard for evaluating HCC histological subtypes. To identify pathological section images of HCC and non-HCC, Chen[21]used a tissue microarray image dataset to pre-train ResNet-34. They employed data augmentation to enhance the model's robustness to color, thereby reducing the significant differences in image rendering caused by staining processes in pathological sections. Typically, different subtypes of HCC imply different patient prognoses, with lower subtype HCC having better prognosis than higher subtype HCC. A study[22]designed a new architecture called LiverNet based on the BreastNet architecture, which effectively captures multidimensional features in HE-stained liver histopathological data by incorporating spatial pyramid pooling modules, convolutional block attention modules, and residual blocks for pathological classification of HCC. Yang[23]used a DL multi-channel fusion three-dimensional convolutional neural network to distinguish HCC of different pathological grades in DCE-MRI images. However, the model performed poorly in distinguishing moderately differentiated HCC (AUC=0.71) and poorly differentiated HCC (AUC=0.64), possibly due to the small sample size and significant differences in cellular structure, vascular invasion, and invasiveness among HCC of different differentiation types.

3. The Application of DL in Postoperative Assessment of HCC

3.1. The Application of DL in the Efficacy Assessment of Transcatheter Arterial Chemoembolization for HCC Patients

Transcatheter arterial chemoembolization (TACE) is a first-line treatment for patients with hepatocellular carcinoma (HCC), but the objective response rate and 3-year overall survival rate in HCC patients remain relatively low[24]. Employing non-invasive methods to assess the survival prognosis of TACE patients and accurately predict their survival can help clinicians make more personalized and refined decisions. Sun[25]developed a deep learning (DL) model to predict survival after TACE based on preoperative CT images, clinical factors, and postoperative responses of BCLC B-stage HCC patients. Although this model has good predictive power, the underlying mechanisms of predicting TACE prognosis are not yet clear and require further in-depth research. Due to the strong heterogeneity of intermediate-stage HCC patients treated with TACE, a study[26]updated the DeepSurv model to the deepHAP IV model to predict the prognosis of intermediate-stage HCC patients, and the deepHAP IV model showed excellent performance in predicting overall survival (with a C-index of 0.74). T2WI-FS imaging and DWI are routine MRI scan sequences, which are easy to obtain and have good reproducibility. Liu[27]established a DL model based on these two MRI sequences to predict the efficacy of TACE in HCC patients, and the results showed that the DL-based nomogram had the best predictive effect. Another study[28]used the EfficientNetV2 software to establish a prognostic model to assess the progression time and overall survival of intermediate-stage HCC patients after TACE treatment, and the results showed that patients with an EfficientNetV2-based prognostic model score ≤0.5 had a better prognosis. However, this study only included intermediate-stage HCC patients, which to some extent limits the scalability of the model.

3.2. The Application of DL in Postoperative Survival Assessment Following HCC Resection, Radiofrequency Ablation, and Liver Transplantation

Image-guided percutaneous thermal ablation (IPTA) is a first-line treatment for early-stage Hepatocellular Carcinoma (HCC) patients. Due to its minimally invasive nature, fewer complications, and good repeatability, IPTA is a suitable treatment option for HCC patients who are not candidates for surgery. Local tumor progression is closely related to tumor activity and invasiveness and is an important risk factor for recurrence after IPTA. Chen[29]addressed this issue by establishing a deep learning (DL) model to predict recurrence after IPTA using quantitative features extracted from multimodal MRI images. The results showed that incorporating multiparameter MRI features of the tumor margin and ablation area can improve the predictive performance of the model. If potential molecular biomarkers (including NLR, MMP7, MUC1, and genetic information, etc.) are included in the study, the accuracy and robustness of the predictive model may be further enhanced. For HCC patients with good liver function, surgical resection is usually the first choice. Although survival rates for HCC have improved in recent years, the overall survival rate remains low. Therefore, postoperative survival assessment for HCC patients after hepatectomy remains important. A study[30] indicated that survival information features are not only extractable from within and around the tumor but also from the entire liver. By designing a fully automated artificial intelligence system based on the entire liver, the study no longer relies on the precision of tumor boundaries, showing great potential in predicting postoperative survival for HCC patients. Liver transplantation is a common method for treating HCC, but recurrence after transplantation is still common. Some scholar[31]used DL methods to detect the transcriptome profiles of recurrent HCC patients to identify differentially expressed genes, related pathways, biological functions, and potential gene characteristics in recurrent HCC after liver transplantation. The results showed that the PI3K/Akt signaling pathway was enriched as a top pathway (WP4172), playing a crucial role in the recurrence process of HCC by coordinating the upregulation of cytokines such as IL6 and IL7 in the tumor microenvironment. The study is limited by a small sample size and incomplete genomic coverage, restricting the research on new genes and pathways related to HCC recurrence. In the future, large-scale genome-wide association studies using next-generation sequencing could be considered to address this issue.

4. Conclusion

DL models hold great potential for early diagnosis, MVI assessment, pathological grading, and prognostic evaluation in HCC patients. However, the poor interpretability of DL models poses challenges for clinical adoption, often necessitating the integration of high-performance modules to enhance interpretability. Future research should consider expanding sample sizes and employing multimodal, multicenter studies, and external data validation to avoid overfitting during training and to improve model robustness and stability. The tumor's surrounding area also contains rich semantic information, and extracting effective features from the tumor's surroundings or the entire liver can often enhance the predictive performance of the model. Currently, the mechanisms by which DL predicts postoperative recurrence and gene-mediated processes in HCC patients remain unknown, and a series of prospective studies will be needed to validate these issues. In summary, while DL models have shown promise in various aspects of HCC management, there is a need for further research to address the challenges of interpretability and to validate their predictive capabilities through larger, more diverse datasets and prospective clinical studies. This will be crucial for translating these models into clinical practice and improving patient outcomes.

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