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A review of medical image-based diagnosis of COVID-19

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Highlights

- Current research on COVID-19 utilizing medical images is categorized into image preprocessing, segmentation, and classification.
- This study provides an in-depth analysis of these categories, as well as provides an outlook on the application and possible future development directions of medical image processing in COVID-19 management.
- Our paper also presents a review of various publicly accessible datasets of COVID-19.

Abstract

The pandemic virus COVID-19 has caused hundreds of millions of infections and deaths, resulting in enormous social and economic losses worldwide. As the virus strains continue to evolve, their ability to spread increases. The detection by reverse transcription polymerase chain reaction is time-consuming and less sensitive. As a result, X-ray images and computed tomography images started to be used in the diagnosis of COVID-19. Since the global outbreak, medical image processing researchers have proposed several automated diagnostic models in the hope of helping radiologists and improving diagnostic accuracy. This paper provides a systematic review of these diagnostic models from three aspects: image preprocessing, image segmentation, and classification, including the common problems and feasible solutions that encountered in each category. Furthermore, commonly used public COVID-19 datasets are reviewed. Finally, future research directions for medical image processing in managing COVID-19 are proposed.

Keywords: Medical image processing, medical image segmentation, diagnosis, preprocessing, COVID-19 dataset

Introduction

COVID-19 is highly contagious and had been a serious threat to human health [1]. Early clinical manifestations are fever and malaise, sometimes with dry cough and dyspnea. However, with the continuous mutation of virus strains, the virulence of the virus decreases, and widespread vaccination leads to the formation of an immune barrier, contributing to an increased proportion of asymptomatic infections. Early recognition of asymptomatic infections is difficult because of their highly insidious nature [2]. To date, a positive result from RT-PCR test remains the primary criterion for diagnosing COVID-19. However, it is worth noting that this method has a high rate of false positives. So, some researchers have started studying the use of medical imaging for diagnosis [3]. It is difficult for inexperienced medical staff to identify potentially infected patients in a timely manner during the outbreak of COVID-19. Therefore, the diagnosis of COVID-19 requires the aid of medical imaging. Among them, CT and X-ray images are the two most common used modalities. Medical image processing has played an active role in combating COVID-19 [4].

This paper aims to extensively discuss the application of medical imaging in the diagnosis of COVID-19 to facilitate future studies. In this review, we present a summary of three key categories involved in the medical image processing-based identification of COVID-19: preprocessing, segmentation, and classification. Then, we provide an overview of several publicly available datasets. Lastly, we propose several directions for future research. This review is

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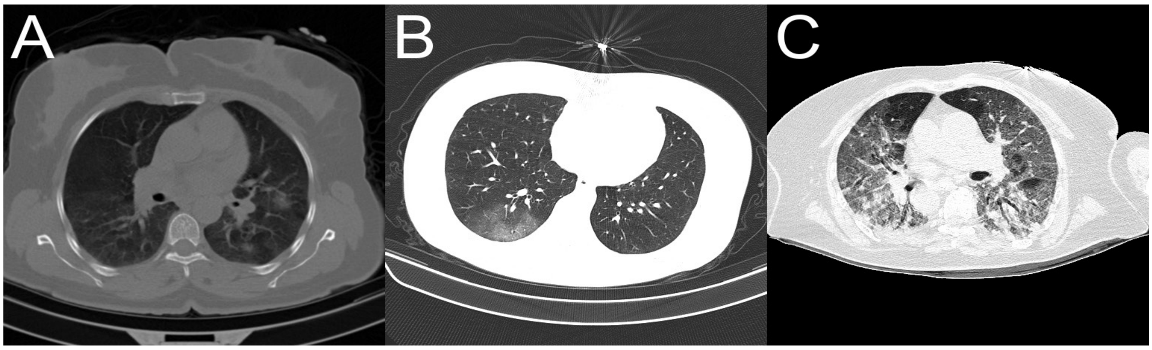

Figure 1. Significant variation among CT images produced by different scanners. (A) Somatom scope; (B) GE Optima CT540; (C) GE Revolution CT. All images were sourced from Shanghai Chest Hospital and have obtained informed consent from the participants.

anticipated to offer valuable insights and guidance for both researchers and radiologists.

Methods

This study examined six databases and other relevant websites, such as National Knowledge Infrastructure, PubMed, IEEE Xplore Library, Science Direct, SpringerLink, and Google Scholar. Diagnostic studies of COVID-19 based on medical images (CT and X-ray images) conducted between 2020 and 2022 were primarily considered. Repetitive studies were excluded, and only representative ones were retained. The search terms encompassed various keywords, including but not limited to "machine learning," "deep learning," "COVID-19," and "SARS-CoV-2." Ultimately, 78 eligible studies were included, covering topics such as segmentation, preprocessing, diagnosis, and datasets of COVID-19.

Preprocessing

Image preprocessing generally encompasses data enhancement and generation. This step serves to reduce image noise, improve the model's generalization performance, mitigate model overfitting, and enhance the detectability of useful information, thereby improving the reliability of the results of subsequent tasks such as feature extraction, image segmentation, and classification.

Data Augmentation

Data augmentation is a widely used technique to address imbalances in dataset distribution and mitigate overfitting of the model, and the its common methods include flipping, rotating, cropping, filling, scaling, panning, as well as contrast and brightness adjustment, which have yield favorable outcomes [5, 6]. In a comparative study conducted by Nishio et al. and aimed at differentiating X-ray images of COVID-19 patients, patients with common pneumonia, and healthy individuals, the accuracy of the model was improved by 4% through using conventional data augmentation techniques [7]. However, the benefits of these data augmentation techniques are limited. Also, different scanners can cause large image variations. As shown in **Figure 1**, images from different CT scanners vary greatly. So, researchers need to design more suitable data augmentation methods according to their datasets. In addition to the problems of image noise and unbalanced distribution, the quality of images produced by different imaging devices often varies widely. Therefore, pre-processing is necessary when multiple datasets are used. In image processing, histogram equalization is often used to increase the local contrast, but it tents to introduces new noise to the image while reducing useful information [8, 9]. This phenomenon arises when specific grayscale levels, which contain valuable information, undergo compression or stretching, resulting in the loss of details or an excessive emphasis on details. Some researchers use a Perona-Malik filter to eliminate the noise introduced by histogram equalization, while more researchers use the method of contrast limited adaptive histogram equalization (CLAHE) [8, 10]. Adaptive histogram equalization (AHE) can amplify the local contrast of an image to obtain more details; however, it also amplifies the noise. CLAHE, on the other hand, reduces the noise by limiting the amplified contrast. Researchers put the images pre-processed by CLAHE into the classification model of COVID-19 images and obtained an excellent accuracy of 94.56%, which significantly improved the classification performance of the network [10]. Lung images processed with the modified clip limit-based contrast limited adaptive histograms equalization (MC-CLAHE) and singular value decomposition-contrast limited adaptive histogram equalization (SVD-CLAHE) approaches both obtained good classification accuracies [11, 12].

Data Generation

It is difficult to obtain a large number of CT images or X-ray image datasets of COVID-19 in a short time due to the specificity of medical datasets and the large amount of manpower required. However, machine learning, especially deep learning, is primarily dependent on a large number of images. Therefore, many researchers used weakly supervised learning methods for COVID-19 detection and diagnosis tasks [13, 14]. Weakly supervised learning is intermediate between supervised and unsupervised learning, and it can obtain favorable results based on a small amount of data.

Generative Adversarial Network

Generative adversarial network (GAN) was used for image denoising and produced high-quality images [15]. The gradient loss function was introduced into unsupervised learning-based non-rigid 3D medical image alignment and exerted favorable results in processing data with noise and blur [16]. The weakly supervised learning method can not only remove noise from the original image to obtain a high-quality image, but also generate new images to expand the dataset. Loey et al. used GAN to expand the original dataset by a factor of 30 and obtained favorable results in diagnosing COVID-19 based on X-ray images [17]. However, the expansion was based on the original small dataset, and the model's generalization performance was not tested. Therefore, the quality of the generated images could not be guaranteed. In a study conducted by Albahli et al., the synthetic chest X-ray images were checked by five radiologists and then mixed with the original images for the diagnosis of COVID-19, and the classification accuracy based on the deep learning network Resnet achieved 89% [18]. However, the original images were all from the frontal angle, and the accuracy may be higher if X-ray images from other angles could be combined. In addition to generating images from the same image pattern, weakly supervised learning enables image style migration and cross-modal data enhancement. Some researchers used GAN to transform contrast-enhanced CT images into non-enhanced CT images and compared the segmentation performance of U-Net trained on the original dataset with that of U-Net trained on the combined dataset of original data and generated images, with the latter accuracy being 4% higher than the former [19]. In the study of Zhang et al., they used 3D Cycle-GAN with a shape consistency loss function to combine two modality datasets with labels and achieved mutual image transformation and data enhancement between cardiac magnetic resonance images (MRI) and cardiac CT images [20]. Still, it requires labels in both datasets, which limits the application scenarios of this approach. Some researchers proposed an end-to-end synthetic segmentation network for training segmentation networks across modalities. With SynSeg-Net, they transformed the labels in MR and CT into each other and achieved better results in segmenting brain CT images and abdominal enlarged spleen [21].

Domain Adaptation

Besides GAN, transfer learning based on domain adaptation is also a kind of weakly supervised learning method for solving the problem of lack of labels. Applying an algorithm or model trained in one or more domains to other domains is called domain adaptation, and the source and target domains need to have the same feature space. Some researchers solved the problem of unlabeled datasets by domain adaptation in COVID-19 diagnosis and obtained favorable outcomes [22, 23]. Jin et al. proposed a self-correcting learning scheme with domain adaptation driven by prior knowledge and dual-domain enhancement and applied it for self-correcting segmentation of infected regions in lung CT images [24]. The model, so called DASC-Net, adaptively aggregates the learned model and the corresponding generated pseudo-labels so that the features of the source and target domains are aligned. This method reduces the generated noise caused by the pseudo-labels. Later, the proposed model was applied on three publicly available COVID-19 CT datasets to test its generalization performance, and the results showed that DASC-Net obtained more advanced segmentation accuracy than others. Sun et al. proposed a novel orthogonal decomposition adversarial domain adaptation (ODADA) architecture for replacing the traditional adversarial domain adaptation module, tested it on three publicly available datasets, and received favorable outcomes [25].

Brief Summary

In this section, the importance of pre-processing is first described, and some common methods are enumerated. Subsequently, a number of countermeasures are presented, along with the corresponding limitations in data augmentation and data generation encountered during medical image processing when dealing with difficult-to-collect datasets and variations in dataset quality during the COVID-19 epidemic. Almost every medical image processing requires preprocessing to achieve higher accuracy. Therefore, we hope that this section can assist relevant researchers in choosing the appropriate preprocessing method according to their datasets, so as to accomplish subsequent tasks more effectively.

Segmentation

Medical image segmentation is to identify regions of interest from medical images (including MRI, CT images, ultrasound images, etc.) and segment them from the background, which is an essential yet challenging step in image processing and analysis for evaluating and quantifying COVID-19 [26-28]. According to the tools used, medical image segmentation can be further divided into traditional and semantic segmentation based on deep learning. In traditional methods, researchers manually extract low-level semantic features such as color values, grayscale values, and geometry of the image and then segment the image into multiple regions without intersection with similar features shared in the same region. Finally, the segmented image is obtained by annotating these regions. The commonly used traditional methods are segmentation algorithms based on thresholding, region, edge detection, configuration, clustering, deformable model, and graph theory. Segmentation based on deep learning extracts the medium- and high-level semantic features from the images. Due to the excellent feature extraction and representation capabilities in image segmentation, as well as the avoidance of manual feature extraction, convolutional neural networks (CNN) have been used to segment medical images in recent years. CNN has made great contributions, especially in segmenting COVID-19 images [28]. But few researchers have conducted research in this direction because there are few COVID-19 X-ray datasets with mask images [29]. The primary focus of this section is to provide a comprehensive summary of the application of deep learning in medical image segmentation, specifically on CT images of COVID-19. Within the existing literature, two distinct segmentation tasks have been identified for the segmentation of COVID-19 images: lung field segmentation and lung-lesion segmentation.

Lung Field Segmentation

Lung field segmentation is to segment the lung from the image as a preprocessing step for subsequent tasks such as classifying and fine segmenting the infected region. Several studies have demonstrated that lung field segmentation helps to improve diagnostic accuracy and reduce the difficulty of the subsequent tasks [10, 29, 30]. In the study of Aswathy et al., cascaded U-Net was employed for segmentation of COVID-19 images [31]. They first removed the part of the background that resembled the lung by preprocessing. After this, they used two 3D U-Net, of which the first network separated the lung from the background, and the second network segmented the lung lesion region, and finally obtained a favorable dice score of 82%. Wang et al. constructed a segmentation-classification dual task model in which the entire parenchymal lung region was firstly segmented, and the lung lesion region was segmented afterward [32]. They tested several combined models of segmentation and classification networks and validated them on multiple datasets by five experts. The result showed that the "3D Unet++-ResNet-50" combined model achieved the best AUC of 0.991, and the system was deployed in at least sixteen hospitals.

Lung-Lesion Segmentation

Lesion region segmentation is to segment regions of interest from lung images, such as regions indicating consolidation, ground glass opacity (GGO), pulmonary fibrosis, interstitial thickening, and pleural effusion. However, lesion regions in CT images of COVID-19 patients at early stage are small and have their own shapes and textures, which are challenging for lesion segmentation. Most segmentation models are variations of U-Net and V-Net. We present a typical segmentation-based COVID-19 diagnosis model in **Figure 2** [33]. U-Net is a fully convolutional network with U-shaped symmetric encoding and decoding paths, and the same layers in both paths are connected to learn contextual features better. Several studies demonstrated the applicability of U-Net to the segmentation of medical images [33, 34]. V-Net is a variant of U-Net applied to 3D data. Zhang et al. proposed a new segmentation method that combined residual and dense blocks and used them in U-Net to form a new concatenation, namely QC-HC U-Net [34]. They tested it on two publicly available datasets and got dice scores of 82% and 81%, respectively. Chen et al. used aggregated residual transformations to learn features with robustness and expressiveness [35]. They applied attention mechanisms to improve the model's ability to distinguish various symptoms of COVID-19, achieving a dice score as high as 94% [35]. Despite the favorable outcomes achieved by countless researchers

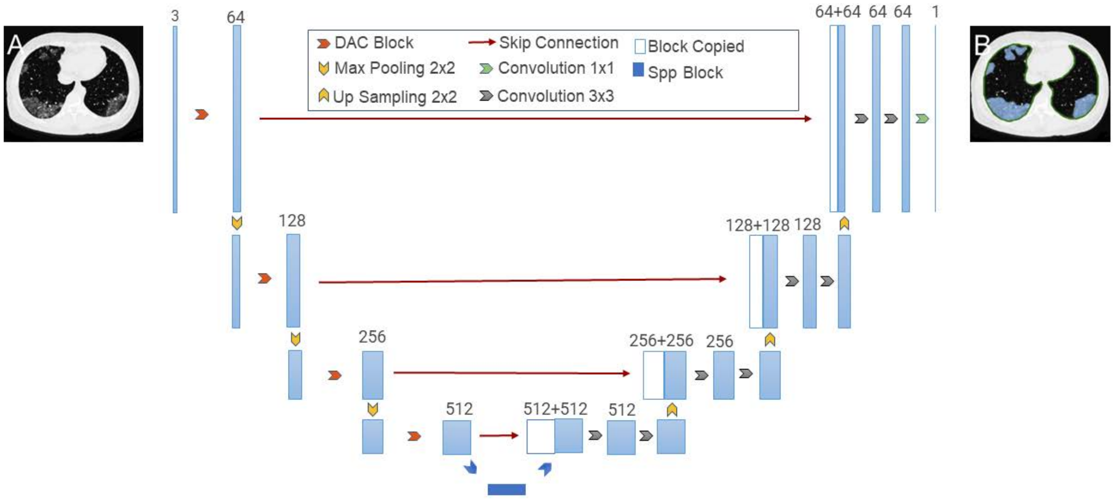

Figure 2. A typical UNet-segmentation-based pixel-level model. (A) original image obtained using the Revolution CT scanner; (B) segmented image obtained using the Revolution CT scanner. This image is from Shanghai Chest Hospital and has obtained informed consent from the participant.

in segmenting medical images using U-Net and its variants, one of the remaining problems of deep learning is the lack of interpretability. Hence, Wu et al. developed a joint classification and segmentation for COVID-19 diagnosis [36]. To increase the interpretability of the model, they introduced class activation mapping (CAM), a tool for visualizing convolutional neural networks (CNNs). Using CAM, they could clearly observe the areas that the model focused on and then make targeted adjustments. Besides, Wu et al. systematically constructed a large COVID-19 classification and segmentation dataset named COVID-CS and tested their proposed system in this dataset segmentation [36]. The dice score of their segmentation task was 78.5%. The lack of labels of datasets is one of the most common problems in medical image segmentation, so some researchers suggested using weakly supervised methods to generate segmentation mask images. In a study conducted by Fan et al., they proposed a COVID-19 lung lesion segmentation network called Inf-Net, which utilized a reverse attention module and an edge attention module to improve the identification of infected regions [37]. In addition, to address the lack of labeling of datasets, they also proposed a semi-supervised segmentation network named Semi-Inf-Net. Wang et al. introduced the self-attentive mechanism and spatial convolution module into the segmentation model (SSA-Net) to automatically identify infected regions from chest CT images [38]. The self-attentive mechanism could extract useful contextual information from deeper levels to enhance feature learning without additional training time. Spatial convolution is a method that processes only the adjacent image elements around each pixel, which can be used to strengthen the network and accelerate the training convergence.

Brief Summary

This subsection provides an overview of medical image segmentation, including its meaning and classification. Additionally, common challenges associated with segmenting COVID-19 images are outlined, and a range of potential solutions are presented. The goal of this subsection is to assist researchers in selecting the most suitable network architecture for their specific segmentation problems and to help them anticipate possible challenges while providing corresponding solutions.

Classification

Rapid identification and appropriate treatment of patients with suspected COVID-19 in the epicenter of outbreak is of great importance. Due to the fast imaging, X-ray and CT scans are widely used to diagnose COVID-19 [39]. However, the large number of medical images adds to the burden of specialists, and COVID-19 shares the same imaging features with common lung diseases such as pneumonia. Inexperienced doctors may need help in distinguishing them. Therefore, it is necessary to use machine learning to assist in classification. In the existing studies, COVID-19 classification based on medical images and artificial intelligence could be broadly classified into three categories: classification based on traditional machine learning, CNN-based classification, and combining of traditional machine learning and CNN.

Classification Based on Traditional Machine

Learning

The common algorithms for the classification task of the COVID-19 dataset mainly include Naive Bayes (NB), support vector machine (SVM), decision tree (DT), random forest (RF), adaptive boosting (AdaBoost), K-nearest neighbor (KNN), gradient boosting decision tree (GBDT), logistic regression (LR), artificial neural network (ANN), extremely trees (ET), light gradient boosting machine, multilayer perceptron (MLP), etc. In a study by Absar et al., the texture, color, and shape features were extracted from 7,180 X-ray images after preprocessing [39]. Then, these images were classified by an SVM classifier with five-fold cross validation, which obtained an accuracy of 98.83%. Wu et al. used a combination of gray level co-occurrence matrix (GLCM) and nonsubsampled dual-tree complex contourlet transform (NSDTCT) to extract texture features of images, and used an RF classifier to predict the result [40]. At last, they achieved an AUC of 0.957 in distinguishing COVID-19 from other pneumonia. Some researchers used a single model, while others selected the optimal model from multiple models or used a combination of models to construct their classification models. Tamal et al. manually segmented lung parenchyma in X-ray images, after which the radiomic features of each lung were extracted separately using a tool called Pyradiomics, and achieved an AUC of 0.9226 in classification task with multiple machine learning algorithms [41]. Shahin et al. developed a computer-aided diagnosis (CAD) program [42]. After being segmented by k-mean clustering, the images were predicted by SVM and radial basis functions (RBF). This program performed well in predicting whether a patient was infected with COVID-19 and staging the patient's condition, and it could be used to reduce the workload of clinicians.

CNN-based classification

The performance of the traditional machine learning approaches is limited, while CNNs can perform better. Diagnosing COVID-19 by transfer learning is one of the most common approaches. It is more challenging to obtain COVID-19 medical image datasets compared to common pneumonia and normal subjects, so if the data used to train the CNN model are unbalanced, especially when there are fewer COVID-19 images compared to other classes, although good results can be obtained in the overall classification task, the performance would be poor in detecting COVID-19 alone. Such classification networks do not have reliability. Data augmentation is the most common solution to the imbalance in data distribution. Saha et al. applied a deep convolutional neural network called decomposition, transfer, and combination (DeTraC) to detect COVID-19 in X-ray images [43]. To improve the efficiency of the model, principal component analysis (PCA) was applied to project the high-dimensional features extracted through the CNN to lower dimensions for feature dimensionality reduction. Finally, their method was tested on two datasets, and obtained an accuracy of 93.1%. The number of common pneumonia images they used was significantly less than that of COVID-19. Although the data augmentation was used to slightly moderate the error caused by an imbalance in the number, they did not take into account the error caused by different image sources. A transfer learning method based on domain adaptation solved this problem well. Zhang et al. used a domain adaptation method called COVID-DA to accurately identify COVID-19 with a small number of labels [30]. Using a single CNN model to detect COVID-19 without model improvement might make it difficult to achieve high-accuracy classification on X-ray images or CT images [44]. Some researchers started to explore the use of multiple deep learning models and combine them in a task, and this learning method is called integrated learning. Rahimzadeh et al. used features extracted through two CNN models (ResNet50V2 and Xception) in tandem for a triple classification task on X-ray images based on two publicly available datasets, and the average accuracy reached 91.4% [45]. Hall et al. applied ResNet50, VGG16, and their own small CNN to the classification task of COVID-19 and selected problematic CT images using a voting system, with a final accuracy of 91.24% [46]. The integrated model using multiple algorithms could improve the accuracy of diagnosis to some extent compared to each individual algorithm, but the integrated model is computationally expensive because it must train millions of parameters, which makes it challenging for researchers to tune the hyperparameters.

Classification Based on a Combination of Traditional Machine Learning and CNN

Some features extracted by CNN may negatively affect the classification task, and we can remove these irrelevant features by combining traditional machine learning algorithms to obtain higher classification accuracy. Many researchers combined traditional machine learning and CNN and obtained favorable outcomes [47]. Sahlol et al. proposed an improved COVID-19 image hybrid classification method using CNN to extract features. They used the

Table 1. Summary of COVID-19 image datasets

Dataset	Modality	Covid-19	Total	Format	Segmentation	Diagnosis
COVID-QU-Ex	X-ray	11,965	33,920	2D	√	√
COVIDGR Dataset	X-ray	426	852	2D		√
COVIDx Dataset	X-ray	16,490	30,882	2D		√
Covid-Chestxray-Dataset	X-ray+CT	563	930	2D		√
BIMCV COVID-19+	X-ray+CT	--	23,527	3D	√	
COVID-19 CT Lung and Infection Segmentation Dataset.	CT	20	20	3D	√	
SARS-CoV-2 CT	CT	1,252	2,482	2D		√
COVID-19 CT Segmentation Dataset	CT	110	110	3D	√	
MOSMEDDATA	CT	--	1,110	3D	√	
COVID-CT Dataset	CT	15,589	63,849	2D		√
CT Scans for COVID-19 Classification	CT	4,001	39,370	2D		√
COVIDx CT	CT	--	431,205	2D	√	√
Large COVID-19 CT Scan Slice Dataset	CT	7,593	17,104	2D	√	√

marine predator algorithm (MPA) to select the most relevant features [48]. Finally, fractional-order calculus (FOC) was used to enhance features. Then, they applied this method to several datasets, and the classification accuracies were all above 98%. Their approach achieved high performance in classification while reducing the computational complexity. Kassania et al. used an advanced CNN model to extract features from X-ray images and trained machine learning algorithms to classify COVID-19 [49]. They used 10-fold cross-validation to evaluate the average generalization performance of the classifier in each trial. Finally, the combination of DenseNet-121 and Bagging Tree achieved an optimal accuracy of 99.00%, which is also the highest accuracy on this dataset. However, their dataset is small, and further validation on a larger dataset is needed. In the study of Jin et al., the pre-trained AlexNet model was used for deep feature extraction and filtered features [50]. Finally, SVM classifiers with various kernel functions (linear, quadratic, cubic, and Gaussian) were used for COVID-19 classification, achieving an accuracy of 98.64%, which was higher than that of the pre-trained CNN classification alone.

Brief Summary

This section provides a detailed introduction to the role of medical image-based classification methods in COVID-19 from three aspects: classification based on traditional machine learning, CNN-based classification, and combining traditional machine learning with CNN. Traditional machine learning technology is comparatively mature but exhibits limited performance, whereas CNNs often yield favorable results but require additional resources. The combination of traditional machine learning and CNN can achieve high classification accuracy.

Dataset

Having sufficient high-quality training datasets is vital for designing, implementing, and evaluating COVID-19 medical image-based diagnostic models. In this section, the focus is on introducing the datasets available for COVID-19 images. **Table 1** provides a summary of 13 datasets used for classification and segmentation purposes. The table includes information such as the imaging modality, the number of COVID-19 samples, the total number of samples, the dimensionality of the data, and suitability for segmentation or classification tasks.

• COVID-QU-Ex dataset [51-55]. This dataset was created by multinational researchers including Qatar University in Doha, Qatar. It contains chest X-ray image data of positive COVID-19 cases as well as normal and viral pneumonia images. The dataset consists of 33,920 chest X-ray images and corresponding masked images, including: 11,956 COVID-19 images, 11,263 viral or bacterial pneumonia images, and 10,701 normal chest images.

• COVID-19 CT lung and infection segmentation dataset [56]. This dataset contains 20 labeled COVID-19 CT scan images. The left lung, right lung and infected areas are segmented by two radiologists and validated by experienced radiologists.

• SARS-CoV-2 CT dataset [57]. The data were collected from patients at the São Paulo Hospital in Brazil, containing 1,252 COVID-19 CT images and 1,230 CT images of healthy subjects.

• Covid-Chest x-ray dataset [58]. The dataset contains 930 images, including 45 lung CT images (including 42 positive images) and 885 x-ray images. The limited sample images dictates that it needs to be used in conjunction with other datasets.

• COVID-19 CT segmentation dataset [59]. The dataset contains 110 CT scan images, 100 of which are annotated by radiologists and labeled with three types, including GGO, consolidation, and pleural effusion. In addition, it contains more than 700 lung parenchymal mask images that can be used to train the whole lung segmentation network.

• MOSMEDDATA [58]. The dataset was provided by the Municipal Hospital in Moscow, Russia, with a total of 1,110 CT scan images, 50 of which have masked images, and the GGO and lung nodules were annotated by doctors.

• COVIDGR dataset [60]. This dataset was collected by the Granada Hospital and contains a total of 852 X-ray images. It is noteworthy that it is a well-balanced dataset, containing X-ray images of both COVID-19 positive and healthy individuals, and covering a wide range of illnesses and various stages of each one.

• BIMCV COVID-19+ [61]. Data were collected from some public datasets, including COVID-CT-Dataset, COVID-19 dataset, COVID-19 radiography database, and some private datasets. It includes a total of 23,527 X-ray and CT images, 23 of which are GGO and solid lung lesions that annotated by radiologists. It is noteworthy that the size of this dataset is 389.27 GB, which can satisfy most of the deep learning dataset requirements.

• COVID-CTset [62]. It was collected from a radiology department located in Sari, Iran, from March 5 to April 23, 2020. The dataset contains complete raw CT scans of 377 individuals, including 15,589 CT images from 95 COVID-19 patients and 48,260 images from 282 healthy individuals.

• CT Scans for COVID-19 Classification [63]. The data were collected from Union Hospital (HUST-UH) and Liyuan Hospital (HUST-LH), containing a total of 39,370 CT images. The researchers manually labeled a subset of 4,001 images with imaging features associated with COVID-19, 9,979 images of both lungs with imaging features unrelated to COVID-19 and excluded 5,705 images that do not contain any lung information. Notably, this dataset also contains some clinical features of the patients that can be used in other studies.

• COVIDx dataset [64]. This is a combined dataset of COVID-19 X-ray images from COVID-19 Image Data Collection, COVID-19 Chest X-ray Dataset Initiative, ActualMed COVID-19 Chest X-ray Dataset Initiative, RSNA Pneumonia Detection Challenge dataset, and COVID-19 radiography database. A total of 30,000 images are included, including 16,490 positive cases.

• COVIDx CT [65]. This is a combined dataset of COVID-19 CT images collected from a number of publicly available datasets, including COVID-19 CT Lung and Infection Segmentation Dataset, MosMed Data [58], COVID-CT Set and so on. A total of 431,205 CT images from 6,068 patients are included.

• Large COVID-19 CT Scan Slice Dataset [66]. This dataset is collected from seven public datasets, including a total of 17,104 images, of which 60 CT scan images have masked images.

Prospect

The medical image-based approach has made an important contribution not only to the diagnosis of COVID-19, but also beyond.

Prognosis

Estimating disease progression or outcome over time based on patients' pre-treatment medical images and guiding decision-making of physicians in further treatment is another area of research in medical imaging. The so-called medical state or outcome can be a specific medical event, such as death complications, or a quantitative measure, such as disease progression, pain and quality of life. In prognostic studies based on medical images, the most common are overall survival (OS) analysis of patients and prediction of disease progression. These prognostic models can provide information for physicians to develop patients' treatment plans. Huang et al. extracted the radiomics features of CT images to predict disease-free survival in patients with the initial stage of non-small cell lung cancer [67]. Ultimately, they found that first-order statistical features were significantly associated with tumor heterogeneity and 3-year disease-free survival, and their method outperformed conventional staging systems and clinicopathologic nomograms. The most common prognostic determination based on medical image of brain is the study of Alzheimer's disease (AD). AD is a progressive neurodegenerative disorder, and interventions in the early stages, known as mild cognitive impairment (MCI) and preclinical stages can obtain more favorable outcome. Accurate prediction of clinical changes in MCI patients, including qualitative changes (when to convert to AD) and quantitative changes at future time points, is therefore important for early diagnosis of AD and monitoring disease progression. Zhang et al. used multiple imaging modalities at multiple time points to predict the conversion of MCI [68]. They applied an MKL classifier consisting of time-varying longitudinal imaging features and patient cognitive test scores at each time point in 88 MCI subjects, 35 of whom converted to AD within one year. After using 10-fold cross-validation, their method achieved an accuracy of 78.4%, outperforming those methods using only single modality images. In addition to AD, some researchers directed their attention to spontaneous intracerebral hemorrhage (SICH). Zhou et al. collected radiomic features from CT images and some clinical information of 326 patients with SICH and developed radiomic-clinical (R-C) nomogram drawings for the short-term prognosis of patients, and finally selected nine features for prognosis prediction [69]. Their method obtained an AUC of 0.80 on the test sets, which helped clinicians assess the risk of patients. In addition to lung and brain, the approach based on medical images performed well in the prognosis prediction of disease in other sites, such as breast, prostate, and liver. Keyl et al. developed a survival prediction model for advanced pancreatic cancer based on machine learning and multimodal data [70]. They extracted clinical data and radiomic features from 203 patients with advanced pancreatic cancer and performed feature selection, resulting in a C-index of 0.71.

Since the outbreak of COVID-19, there has been a shortage of medical resources in many places of the world. If emergency resources are deployed properly, the epidemic can be effectively controlled; otherwise, it will inevitably cause great losses. Therefore, during an epidemic, it is particularly important to manage patients in a hierarchical manner and to plan the use of medical resources such as the ICU. Zhang et al. proposed an AL-based radiomic nomogram, and they used CT images and clinical information to prognosticate the subsequent condition of COVID-19 patients [71]. They finally selected 21 radiological features and two clinical features that were significantly associated with COVID-19 prognosis, and validated these features on an external dataset with favorable outcome (an AUC of 0.84). In addition to CT images, several studies have shown the statistical relevance of chest X-ray images for predicting the subsequent progression of COVID-19 for the hierarchical management of patients. Younus et al. proposed a novel high-resolution CT (HRCT) scoring system for predicting the progression of COVID-19 patients [72]. They divided the two lungs in CT images into 20 regions, scored each region, and graded COVID-19 patients according to the scores and clinical parameters for the hierarchical management. Their method, to some extent, reduced the burden on medical institutions during an epidemic. However, due to the scarcity of relevant datasets and patient privacy, prognostic studies based on medical images of COVID-19 patients are rare. Most of the studies do not have generalization performance and are all short-term research. Studies have shown that some COVID-19 patients develop a variety of medium- and long-term sequelae after initial recovery from COVID-19, which may affect the respiratory, cardiovascular, neurological, musculoskeletal, dermatologic, and renal systems [73]. For this reason, the World Health Organization has emphasized the importance of the medium- and long-term prognosis management for patients with COVID-19. A prognostic approach based on medical images may help physicians predict patients who are prone to develop COVID-19 sequelae early, so as to make treatment plans in advance.

Efficacy Assessment

Clinical efficacy assessment aims to examine the safety and efficacy of a drug or a treatment method in patients. Evaluation of effectiveness by comparing the differences in images before and after treatment is a typical approach. The WHO criteria and the Response Evaluation Criteria in Solid Tumors (RECIST) are the golden criteria for assessing the effectiveness of radiation therapy in eliminating tumors, and tumor size is one of the most important factors in these two criteria. Mena et al. used PET-CT to monitor the condition of NSCLC patients treated with radiation therapy [74]. They evaluated the efficacy according to the size of the tumor before and after treatment and made targeted adjustments to the subsequent treatment plan. The results showed that PET-CT images could be evaluated systemically, and they played an important role in all stages of treatment (diagnosis, initial staging, treatment response assessment, and recurrence monitoring) in patients with NSCLC. Hadi et al. predicted the outcomes of breast cancer patients after neoadjuvant chemotherapy (NCA) with breast ultrasound images and the KNN classifier [75]. They extracted textural features from ultrasound images of 100 patients before, one week after, and four weeks after treatment, and combined clinical, pathological, and 5-year relapse-free survival (RFS) information to develop an efficacy assessment model for evaluating the outcome of patients after receiving NCA. Ultimately, their model obtained an accuracy of 96%. Medical image-based efficacy assessment can help healthcare professionals evaluate the effects of therapeutic modalities such as radiation therapy, targeted therapy, and immunotherapy, as well as certain drugs. Mejia et al. evaluated the efficacy of drugs on patients with heart muscle disease by echocardiographic monitoring [76]. A comparison of parameters such as ventricular geometry, left ventricular end-diastolic dimension, and ventricular function in patients with dilated cardiomyopathy at pre-treatment, six months post-treatment, and 18 months post-treatment revealed that cardiac reverse remodeling drugs were highly effective in treating dilated cardiomyopathy, while Beta-blocking drugs reduced the patient's heart rate and increased diastolic filling time for cardiac hypertrophy, decreasing left ventricular outflow tract flow.

According to relevant studies, the mortality of COVID-19 patients in severe or critical conditions could be as high as 49%, and respiratory support and dexamethasone use remain the mainstay of treatments [77]. Therefore, scientists are investigating the development of other drugs and treatment modalities to reduce the rate of severe illness and mortality in patients with COVID-19. In the process of developing new drugs or treatment modalities, it is particularly important to select appropriate efficacy assessment metrics. To evaluate the effectiveness of antiviral therapy in patients with COVID-19, Liao et al. designed a simulation trial to assess the efficacy of Remdesivir in patients with COVID-19, and the results demonstrated that Remdesivir helped to reduce mortality and improve the chances of recovery [78]. However, their trial included only statistical data, such as the length of hospitalization and mortality of patients, but ignored clinical and physiological data during treatment. Tobback et al. designed a randomized controlled trial to assess Camostat's efficacy in COVID-19 patients in severe or critical conditions [79]. They divided 90 patients into two groups. The experimental group was treated by using Camostat, and the control group was injected with a placebo. They used clinical parameters, clinical-improvement time, and nasopharyngeal viral load as indicators for evaluation. Although the final result showed that Camostat was not found to be effective in the treatment of COVID-19 patients, their method still made sense. For the therapeutic drugs or treatment modalities of COVID-19, most of the existing efficacy assessment trials used outcome, clinical, and pathological data as evaluation indicators. However, some studies showed that medical images could also be used for efficacy assessment. In order to evaluate the therapeutic effect of Chinese medicine on patients with COVID-19, Wang et al. selected 55 critically ill patients as experimental subjects [80]. They compared the differences in CT images of patients before and after treatment and established a scoring system for the patients' CT images, which was based on the percentage of lesion area and the type of imaging signs. Higher score indicates more severe disease. Patients' images showed a significant reduction in lung consolidation after Chinese medicine treatment, indicating that Chinese medicine has an important role in promoting lung lesion absorption. It's challenging to collect sufficient high-quality medical image datasets, so many medical image researchers could only obtain data from retrospective trials. However, for efficacy assessment, we have to use different images in each trial due to individual differences, lack of normative indicators, and differences in treatment modalities and drugs, which poses an even greater challenge for research.

Brief Summary

In this subsection, we focus on discussing the potential application prospects of medical images technology regarding both prognosis and efficacy assessment of COVID-19. Additionally, some challenges encountered in existing studies are outlined. However, with the continuous expand of datasets and constant improvement in related standards, medical image-based prognosis, and efficacy assessment will play an increasingly significant role. These methods will aid in predicting subsequent disease progression of COVID-19 patients, assisting medical staff in efficiently allocating medical resources, and evaluating the effectiveness of new drugs.

Conclusion

In this review, recent research on COVID-19 diagnosis based on medical images is summarized in terms of three categories: image preprocessing, image segmentation, and classification. Firstly, the meaning and classification of the three tasks are described, followed by an enumeration of common issues in diagnosing COVID-19 and a presentation of potential solutions. Subsequently, various public datasets for COVID-19 classification and segmentation are introduced. Finally, future research directions for utilizing medical images in combating COVID-19 are proposed.

High-quality medical datasets with sufficient samples are becoming increasingly crucial. In addition to the need for legal and regulatory support, the datasets used by researchers should include different phases and multimodal images, such as ultrasound, X-ray, CT scans, and MRI, whenever possible, due to the fact that such multimodal systems can take full advantage of the important features of each imaging technique, thus improving the reliability of the diagnosis of COVID-19. There are many indications that medical image processing will play an increasingly important role in the future fight against COVID-19.

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