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Chapter 2

Characterizing acute respiratory distress syndrome in COVID-19: a narrative review of artificial intelligence-based lung analysis

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COVID-19 has infected millions of people and caused hundreds of thousands of deaths worldwide. One of the most serious complications of COVID-19 is acute respiratory distress syndrome (ARDS), which can be fatal. People who are at least 60 years old or have underlying health conditions are at higher risk of developing ARDS.

Medical imaging, such as computed tomography (CT) scans and chest x-rays, can be used to diagnose ARDS. However, these tests can be time-consuming and require specialised equipment. Artificial intelligence (AI) is being developed to automate the diagnosis of ARDS from medical images.

AI-based systems can be used to quickly and accurately identify patients who are at risk of developing ARDS. They can also be used to monitor patients who have already developed ARDS and to assess the severity of their condition.

AI-based systems are still under development, but they have the potential to improve the diagnosis and treatment of ARDS. By automating the diagnosis of ARDS, AI can help to reduce the time it takes to get patients the treatment they need. AI can also help to improve the accuracy of diagnosis and to identify patients who are at risk of developing ARDS.

The use of AI in the diagnosis and treatment of ARDS is still in its early stages, but it has the potential to revolutionise the way this serious condition is managed.

2.1 Introduction

In December 2019, a new coronavirus called severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) [1] emerged in Wuhan, Hubei province, China. Initially referred to as novel coronavirus pneumonia (NCP) by the Chinese government [2], it was later renamed coronavirus disease 2019 (COVID-19) by the

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World Health Organization (WHO). COVID-19 is currently a global pandemic [4] and primarily affects the respiratory system, potentially leading to acute respiratory distress syndrome (ARDS) and death. As of December 21, 2020, there have been over 77.4 million reported cases of COVID-19 worldwide, resulting in 1.7 million fatalities [5]. The virus has a high Ro value, ranging from 2.43 to 3.10, indicating its high level of contagiousness [6]. Figure 2.1 illustrates the distribution of reported cases per million population worldwide, with colors ranging from white to dark red. The countries with the highest mortality rates include France, Brazil, Mexico, Italy, the USA, India, the UK, and Spain [7]. It is worth noting that COVID-19 is considered a syndemic, as it involves both biological and social factors [3].

From a genetic standpoint, COVID-19 is found to be more closely related to SARS-CoV-1 rather than the MERS-CoV. However, it is different from SARS-CoV-1 in terms of clinical severity, incubation period, and transmissibility [8]. Despite various government measures such as social distancing, mask-wearing, quarantine, and non-pharmacological preventive treatments for overall well-being, the global spread of COVID-19 has continued to increase [9, 10].

COVID-19 exhibits distinct imaging characteristics and affects organs beyond the lungs [11, 12]. Consequently, there has been an exponential increase in research on COVID-19, with nearly 72 000 related articles published since December 2019, averaging 2000 articles per week (as seen on the PubMed website) [13]. Notably, over 900 articles focus on the intersection 2 of COVID-19 and artificial intelligence (AI), encompassing machine learning (ML), transfer learning (TL), and deep learning (DL) models (as shown in figure 2.2(d)). AI has the potential to aid in the characterization of ARDS in the lungs and the diagnosis of COVID-19's impact on other parts of the body [14]. Careful investigation of AI for ARDS

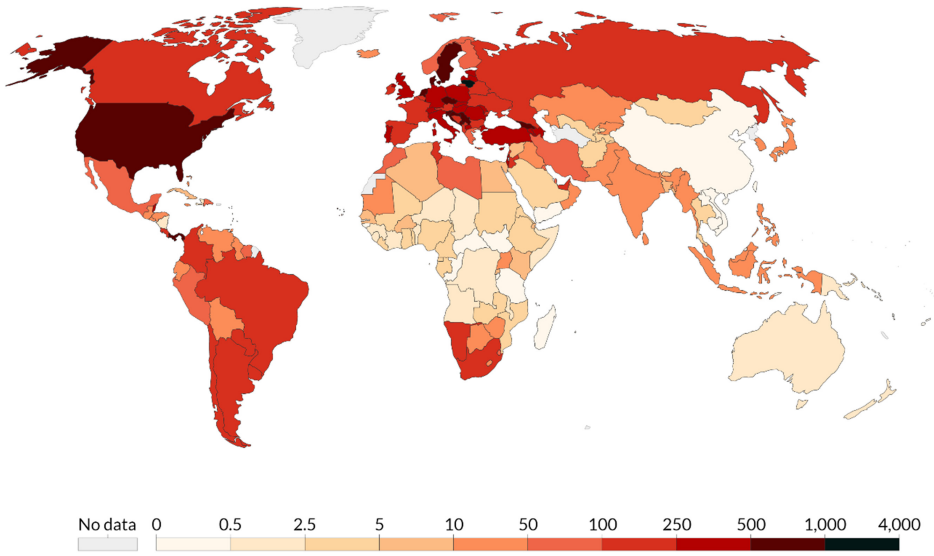

Figure 2.1. Total confirmed cases per million as of December 21, 2020 [15]. (Source: Center for Systems Science and Engineering (CSSE) at Johns Hopkins University, Maryland, USA.).

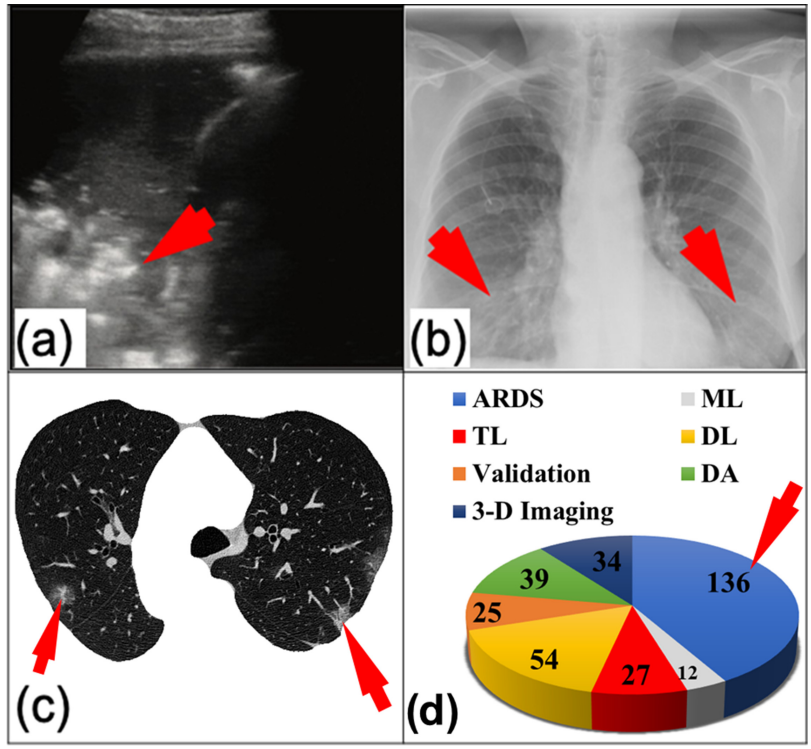

Figure 2.2. Images of COVID-19 infection: (a) lung ultrasound (hyper-echoic region of the COVID-19 lung), (b) chest x-rays (the infected region in the lung), and (c) lung CT (segmented lung region; courtesy of Luca Saba, University of Cagliari, Italy). (d) The number of COVID-19 studies involving ARDS, ML, TL, DL, validation, data acquisition (DA), and 3D imaging.

characterization is essential to assist healthcare practitioners in managing COVID-19 pneumonia and its progression to ARDS.

AI plays a significant role in the management of COVID-19, including patient follow-up, risk assessment, medical imaging, and telemedicine [16]. While AI has been applied in radiological imaging for tasks like classifying images into control, community viral pneumonia, and COVID-19 pneumonia [18–20], it remains unclear if these models align with the expectations of critical care physicians and pulmonologists. Can AI effectively incorporate information on a patient's pre-existing conditions, age, and lung scan patterns to correlate them with the severity of COVID-19? Additionally, there are important questions to address, such as the suitable imaging modalities for ARDS, optimal image-based classifiers for classifying and detecting ARDS severity considering age and comorbidity, estimating patient survival, methods for measuring severity of COVID-19 due to ARDS, assessing the impact of pre-existing conditions on ARDS mortality, and detecting and classifying early stages of ARDS. Addressing these issues is crucial for accurate diagnosis and evaluation of AI-based therapeutic applications [14].

The main imaging tools used for lung imaging include CT, x-rays, ultrasound, and a combination of PET and CT to visualise lung function [21–23]. This study examines different AI-based solutions for classifying COVID-19 lung severity, considering TL, DL, ML, and their combinations. It also highlights important issues that current AI-driven COVID-19 research should tackle in order to provide valuable contributions to the medical field.

This review makes several contributions. Firstly, it explores the pathophysiological aspects of COVID-19-induced ARDS, specifically examining the stages leading to gas-exchange disorders in the alveoli. Secondly, it links comorbid conditions derived from numerous studies to ARDS, including diabetes, hypertension, chronic kidney disease, obesity, cardiovascular diseases, hyperlipidemia, liver disease, cancer, renal dysfunction, HIV, cerebrovascular disease, and lung disease. It also establishes the connection between comorbidity, mortality, and ARDS. Thirdly, it examines the contrast between AI methods employed for characterizing lung diseases before the COVID-19 pandemic (non-ARDS periods) and those utilized during ARDS periods. Fourthly, it introduces seven distinct approaches, referred to as schools of thought (SoT), that utilize AI techniques to assess the severity of COVID-19 within the context of ARDS. Fifthly, it presents a comparative examination of various imaging modalities used for evaluating lung conditions in ARDS. Lastly, it demonstrates how the integration of AI with ARDS and comorbidity contributes to the advancement of personalized medicine, offering valuable insights into assessing ARDS conditions within the framework of COVID-19.

The study is structured as follows: section 2.2 presents the research strategy, section 2.3 describes the pathophysiology of ARDS, section 2.4 analyses the impact of comorbidity in COVID-19, section 2.5 discusses AI architectures categorised into SoT, section 2.6 explains the practical aspect of AI for COVID-19, and sections 2.7 and 2.8 provide critical discussion and conclusion, respectively.

2.2 Research strategy

Figure 2.3 depicts the flowchart of the research strategy adopted in our paper. We conducted research using four online databases: IEEE Xplore, PubMed, Web of Science and ArXiv. Initial screening used the keywords ‘COVID-19,’ ‘coronavirus,’ or ‘ARDS,’ with the modality terms ‘lung CT,’ ‘x-ray,’ or ‘ultrasound.’ The search was augmented with terms ‘artificial intelligence,’ ‘machine learning,’ or ‘transfer learning,’ or ‘deep learning,’ resulting in 1557 articles. We eliminated 115 duplicate articles and those that were not focused on COVID-19 severity, including classification, leaving us with a total of 1442 articles. From these, we further refined our selection based on relevance and novelty, resulting in 399 articles. We excluded articles that were not relevant to comorbidity, resulting in 242 articles. After removing records with insufficient data, we ended up with a final set of 230 resources. These resources were used in our narrative study, which incorporated AI-based, comorbid-based, and pathophysiology-based articles.

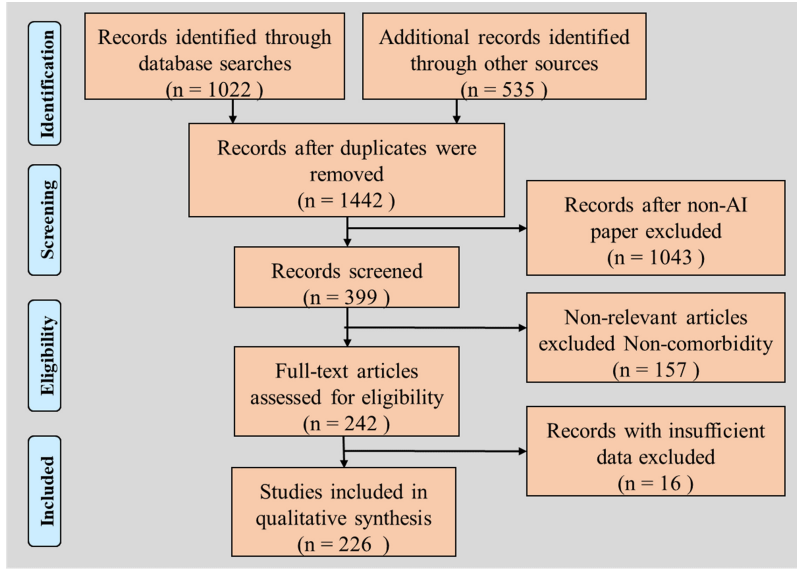

Figure 2.3. The flowchart showing the research strategy.

2.3 The pathophysiology of acute respiratory distress syndrome

The primary mode of transmission for the SARS-CoV-2 virus is through nasal droplets and saliva of an infected person [19]. Upon entry into the body, the virus targets the alveolar type 2 cells (AT2 cells) by binding its viral spike proteins (S1 and S2) to the angiotensin-converting enzyme 2 (ACE2) receptor [24], as depicted in figure 2.4. Previous research by Mossel *et al* has indicated that the SARS-CoV-1 coronavirus exhibits more aggressive replication in AT2 cells compared to alveolar type 1 cells (AT1 cells) in the lung [25]. SARS-CoV-2, with an 80% genetic similarity to SARS-CoV-1, has been shown, via molecular pathways [26], to possess a significant affinity for binding [27]. In the inflammatory phase (termed phase 3), systemic inflammatory mediators are released as a response to SARS-CoV-2 infecting alveolar type 2 (AT2) cells on the surface of the alveolar epithelium [28]. These inflammatory mediators stimulate alveolar macrophages, leading to the production of cytokines such as IL-1, IL-6, and TNF-α. This elevated cytokine production, along with the release of chemokines, can trigger a condition known as a cytokine storm. The sequential occurrence of the systemic inflammatory response, cytokine storm, and organ failure significantly impacts the pathophysiology of ARDS. Similar sequences have been observed in other coronaviruses, including MERS-CoV and SARS-CoV-1 [29, 30]. These processes contribute to the increase in trypsin.

Moreover, the inflammatory response induced by SARS-CoV-2 infection affects the integrity of zonula occludens and endothelial tight junction proteins, leading to weakening and disorganization of endothelial cells. Consequently, the vascular permeability of these cells is increased, allowing intravascular fluids to leak into the

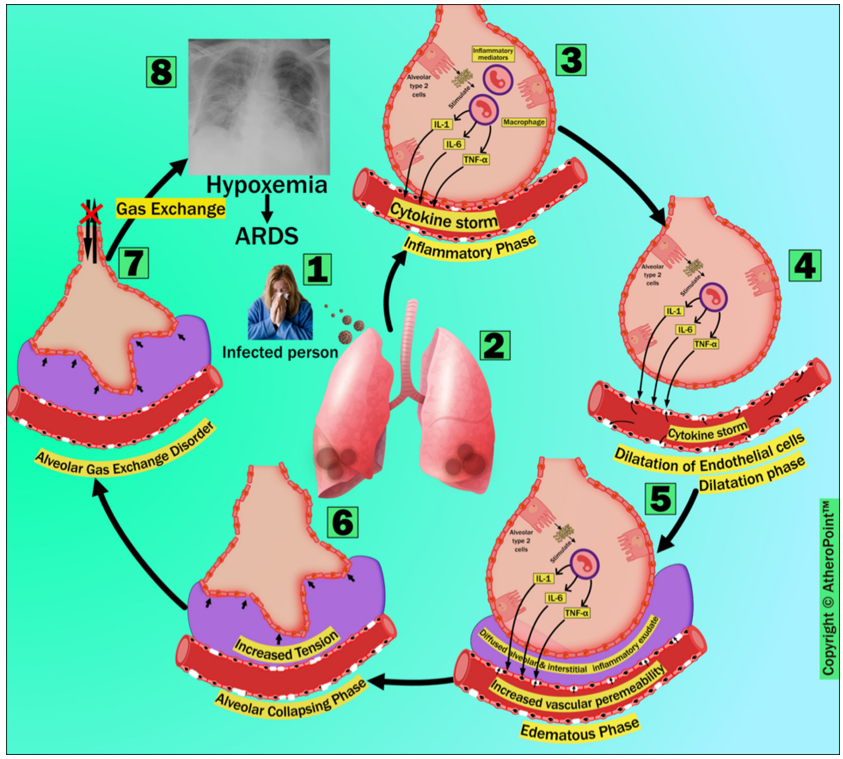

Figure 2.4. The pathophysiology of ARDS after COVID-19 infection, which consists of six phases: (i) inflammatory phase, (ii) dilatation phase, (iii) edematous phase, (iv) alveolar collapsing phase, (v) gas-exchange disorder, and (vi) hypoxemia. (Courtesy of AtheroPoint™, Roseville, CA, USA; reproduced with permission.)

surrounding tissues [31]. During the dilatation phase (referred to as phase 4), the cytokine storm disrupts the endothelial barrier function, which is a consequence of cytokine release following viral infection. This dysfunction contributes to increased vascular permeability. In the edematous phase (designated as phase 5), the elevated intravascular permeability results in the movement of fluids due to diffusion (including neutrophils, proteins, platelets, and erythrocytes) from the blood vessels into the sub-alveolar and interstitial spaces, resulting in the development of diffuse alveolar and interstitial exudates, along with alveolar edema. These manifestations can be detected through radiological consolidations observed in lung CT scans, aiding in the diagnosis and monitoring of treatment response [32]. ARDS is characterized by the presence of diffused alveolar and interstitial exudates, accompanied by elevated sub-alveolar edema [33].

In the alveolar collapsing phase (referred to as phase 6), the accumulation of fluid in the sub-alveolar and interstitial space leads to increased tension, causing the collapse of alveoli. Consequently, the disrupted alveolar structure hinders efficient gas exchange [34]. The alveolar collapse contributes to a ventilation-to-perfusion mismatch between carbon dioxide and oxygen, resulting in impaired gas exchange.

This condition, known as alveolar gas exchange disorder (designated as phase 7), leads to hypoxemia and the development of acute respiratory distress syndrome (ARDS) [35]. If left untreated, the progression of ARDS can increase mortality rates.

2.4 Comorbidity and ARDS

Comorbidities commonly associated with COVID-19 in the context of ARDS include factors such as old age, ethnicity, hypertension, diabetes mellitus (DM), elevated body mass index (BMI), cardiac diseases, and respiratory disorders. Research has indicated that ARDS tends to have more severe outcomes in older patients [36–38], African Americans (Black people in general) [39], individuals with hypertension [36, 40], diabetes [36, 38, 41], higher BMI [42–44], respiratory diseases [42], and myocarditis [45–47]. The inclusion of comorbidities is vital in classifying AI models that can be trained separately to improve diagnosis and predict COVID-19 severity. The cited comorbidity studies [48–101] were sourced from the website https://pubmed.ncbi.nlm.nih.gov/. Figure 2.5 visually presents the number of subjects with comorbidities included in the ARDS-focused studies.

During the selection process, we applied specific criteria based on keywords such as diabetes, hypertension, obesity, cardiovascular diseases, chronic kidney disease, liver disease, renal dysfunction, cancer, hyperlipidemia, human immunodeficiency virus (HIV), cerebrovascular disease, and lung disease. These keywords were utilized to identify relevant studies discussing comorbidity and age groups. 48 studies from specialized medical journals were chosen, provide a rationale and inspiration for gathering statistical data to support the development of innovative AI solutions for the monitoring and diagnosis of COVID-19 severity. Figure 2.6, presented as a pie chart, illustrates the percentage of comorbidity subjects among the selected studies. It is noteworthy that these studies primarily focused on comorbidity and age groups. Among the contributing factors, diabetes and hypertension were identified as the

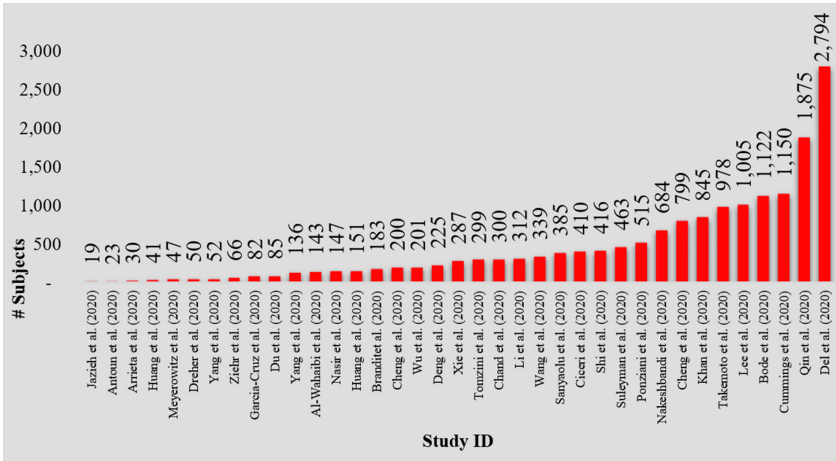

Figure 2.5. The number of subjects enrolled in the ARDS-based studies that consider comorbidities.

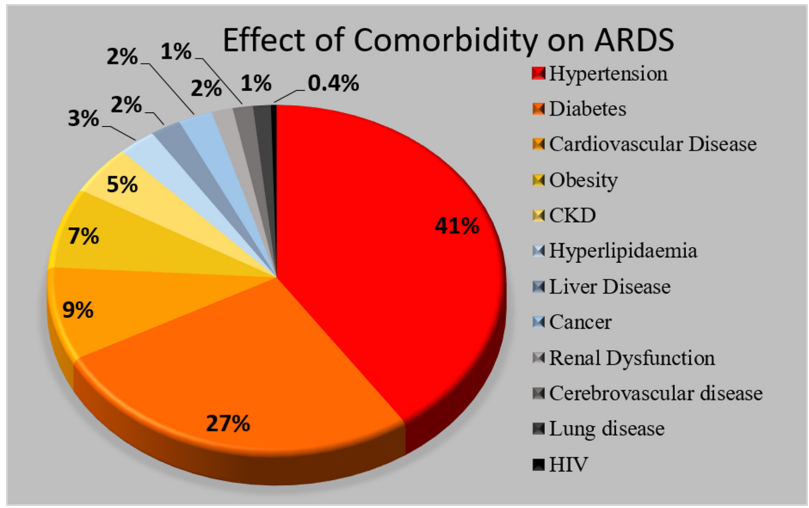

Figure 2.6. Depiction of comorbidities collected from 48 studies.

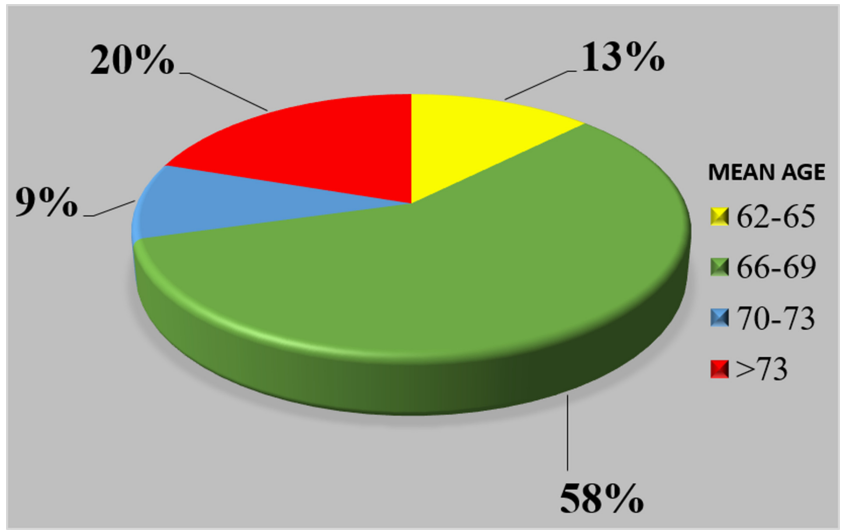

Figure 2.7. Mortality due to the age factor (in years) with comorbidities in the cohort from the selected studies.

two most important comorbidities, accounting for approximately 68% of the cases. The remaining comorbid predictors exhibited similar percentages, ranging from 4% to 13%. According to the selected studies, comorbidities were responsible for 14% of the total deaths in the ARDS framework. This pie chart emphasizes the significant role played by comorbidities in mortality across the cohort. Furthermore, Figure 2.7 illustrates the distribution of deaths caused by a combination of age factors and one comorbidity, at least, within the cohort. The age range with the highest impact was identified as 66–69, comprising 58% of the overall cohort, which is followed by the

age group above 70, which constituted 20% based on the studies included in the analysis.

All the subjects included in the cohort had COVID-19 along with one or more comorbidities. These comorbidities were found to contribute to the deterioration of COVID-19. Consequently, each comorbidity depicts a distinct category within the cohort, with similar grayscale features or imaging characteristics. This observation suggests the possibility of developing multiple knowledge-based AI systems, each trained independently on cohorts specific to a particular comorbidity. By utilizing these independently trained AI systems specific to each comorbidity, it becomes possible to analyze lung scans and evaluate COVID-19's severity.

2.5 Artificial intelligence architectures for ARDS characterization by school of thought

The application of AI in disease characterization has been embraced across various medical imaging domains. This encompasses the role of AI in identifying diseases, extracting the region of interest (ROI) related to the disease, and automatically classifying the disease based on binary or multiclass events. We have selected machine learning and deep learning characterization systems that align and harmonize with ARDS frameworks. The purpose of employing this characterization system is to leverage the creative and innovative approaches developed for various modalities, organs, or applications, fostering knowledge exchange and advancement. It should be noted that certain examples mentioned are from our own research group, deliberately selected to emphasize the significance of tissue characterization and disease characterization through the utilization of AI models. These unique and exclusive solutions serve as a 'one-stop-shop' for researchers interested in understanding the relationship between ARDS paradigms and other organ paradigms. This cluster also provides direct access to our group for more detailed information on parallel characterization systems. AI-based characterization has been applied to various body and disease applications, including the brain [102–104], stroke [105–107], vascular plaque [108–110], arrhythmia [111], liver [112–114], coronary artery [115, 116], prostate [117], ovarian [118, 119], diabetes [120], thyroid cancer [121], skin cancer [122, 123], heart [124–126], rheumatoid arthritis [128], and gene expression [127]. This framework of characterization can be expanded and applied within the context of ARDS.

Regarding studies comparing non-ARDS and ARDS, research specifically focused on ARDS started after December 2019, whereas lung segmentation and classification techniques for non-ARDS cases had been in existence for several years before SARS-CoV-2 emerged. Certain AI models that were initially developed for non-ARDS lung data have been partially investigated and adapted for ARDS lung data. In table 2.1, we present studies conducted in ARDS and non-ARDS frameworks, specifically focusing on segmentation, classification, and sub-regional applications such as cancer, tumor segmentation [129–136], and nodule. Please be aware that we excluded animal studies and lung cellular images, specifically concentrating

Table 2.1. AI-based studies involved during Non-ARDS and ARDS periods. AI-based Non-ARDS: AI on ARDS lung data during pre-COVID-19. AI-based ARDS: AI on ARDS lung data postmarked December 2019 COVID-19 (post-COVID-19).

Subsystems	AI-based Non-ARDS	AI-based ARDS
Segmentation	Characteristics Watershed, region-based, contour-based, fusion-based, and model-based. References [129, 137–146]	Characteristics FC-Densenet103, Unet, DenseNet, and DenseNet121-FPN. References [147–165]
Classification	Characteristics Grayscale feature extraction and ML classifier, and model-based techniques. References [166–170]	Characteristics ResNet50, CNN, SVM, ResNet101, VGG16, and VGG19. References [148, 150–153, 157–159, 171–175]
Joint segmentation and classification	Characteristics They use the same characteristics as adapted by segmentation and classification domain for AI-based Non-ARDS. References [167, 169, 170]	Characteristics They use the same characteristics as adapted by segmentation and classification domain for AI-based ARDS. References [148, 150, 151, 154, 156–159, 162]

on human lungs. Furthermore, validation and inter- and intra-observer variability studies were not considered in table 2.1.

It is important to highlight the three key components of an AI-based ARDS system: lung region segmentation, classification, and COVID-19 severity measurement (refer to table 2.2). In this narrative review, we propose a classification of the literature based on different AI architecture categories, referred to as schools of thought (SoT), as outlined in table 2.3.

AI architecture classification has had a significant impact in numerous engineering domains, especially in medical imaging. Biswas *et al* [17] have examined a specific category of AI architectures for medical imaging, while our study demonstrates the application of various architecture classes (SoT). Biswas also delves into the evolution of architectures within the realm of deep learning and its potential for the present and future.

In the past, both manual and automated feature selection methods were utilized in AI architectures. Manual feature selection involved hand-picking specific features and feeding them into the classification model during the learning and training process. This approach belonged to an older generation of methods and represented

Table 2.2. Types of artificial intelligence architectures and severity index.

	AI components and attributes		
	Lung segmentation	AI component	Severity index
SN	Auto/semi-auto	ML/DL/TL/DL+ ML/DL+TL	Categorical/continuous/ Categorical + continuous
1	Auto	DL	Categorical + continuous
2	Auto	DL+ML	Categorical + continuous
3	Auto	DL	Categorical
4	Semi-Auto	DL+ML	Categorical + continuous
5	Auto	ML	Categorical + continuous
6	Auto	DL+TL	Categorical
7	Auto	TL	Categorical

+: both technologies are present.

a traditional school of thought. However, with advancements in AI, the concept of deep learning emerged, which aimed to mimic the brain by using a greater number of layers to filter features. DL paradigms, characterized by their ability to automatically compute millions of training parameters, represent a more recently evolved subset of machine learning. These methods belong to a newer school of thought, primarily defined by their foundational architecture.

While the AI industry has been predominantly dominated by DL and manual feature selection methods, alternative architectures are continuously being explored. DL, which has been widely used, is starting to show limitations, particularly during training. As a result, new architectures have emerged to address these challenges. One such architecture is transfer learning, which involves generating pre-trained weights to expedite and simplify DL systems. Transfer learning is considered a more recent school of thought and is regarded as a classic in its category. The classification of AI architecture has evolved to align with different schools of thought based on the components and characteristics of the architecture. This approach is similar to how image segmentation was categorized into various architectures or schools of thought in the past. For instance, segmentation was classified as region-based, contour-based, or knowledge-based. These categories were then fused together to create intermediate architectures, known as fused architectures, that combined regions with contours or regions with knowledge. This generation of fused architectures represented another architectural paradigm or school of thought. This concept can be observed in the seminal papers by Suri [176–178].

In the context of AI architecture, the term 'School of Thought' (SoT) is synonymous with architectural design. Each individual architecture, as well as fused architectures, can be considered as a distinct SoT. Fused architectures have been developed by various research groups worldwide and have been documented in the literature. Therefore, the SoT represents a more refined approach to architectural

Table 2.3. Clustering of multimodality artificial intelligence architectures and their salient features.

SoT	Reference	Modality	3D/2D imaging	Highlight/objective	Architecture description	Performance metrics
SoT-1	[147–153, 229]	CT: [147, 148, 229] X-ray: [149, 151] LUS: [150]	3D: [147, 148, 229] 2D: [149–151]	Multiview fusion [229], Multiview pyramid network with attention [147], training using human in loop [148], video-based real-time prediction [150], end- to-end DL architecture for semi quantitative prediction COVID- 19 severity [151]	ResNet50 [229], Custom CNN with attention [147], VB-Net [148], commercial deep learning system by Lunit Inc [149], Spatial Transformer Net- work [150], ensemble of multiple networks (Backbone—ResNet, VGG, DenseNet, Inception; Segmentation-UNet, UNet++; Alignment-Spatial Transformer Network; Scoring Head-Feature Pyramid Network; Custom Network) [151]	ACC: [147, 148, 150, 151, 229] AUC: [147, 229] Sensitivity: [149, 150, 229] Specificity: [149, 229] Others: [148–151]
SoT-2	[152, 153]	CT: [152, 153] X-ray: LUS:	3D: [153] 2D: [152]	Biomarker based model [152], model for severity in 3D lung abnormalities [153]	ResNet34 with logistic regression [152], Dense UNet [153]	AUC: [152] Others: [152, 153]
SoT-3	[154–156, 171, 173, 174]	CT [154–156, 171, 173] X-ray: [157, 174] LUS: NA	3D: [154, 173] 2D: [155–157, 171, 174]	3D Convolution Network [154], multi-objective differential evolution based CNN [171], comparison of ten CNNs [156], weakly supervised DL model [173], truncated InceptionNet [174], modified DarkNet CNN [157]	ResNet50 [154], Custom CNN [157, 171, 173], DenseNet [155] (AlexNet, VGG16 VGG19, SqueezeNet, GoogleNet, MobileNet-V2, ResNet18, ResNet-50, ResNet101, and Xception) [156], InceptionNetV3 [174]	ACC: [155–157, 171, 173, 174] AUC: [154–156, 173, 174] Sensitivity: [154–157, 171, 173, 174] Specificity: [154–157, 171, 173, 174] Others: [155–157, 171, 173, 174]

SoT-4	[157]	CT: [157] X-ray: NA LUS: NA	3D: [157] 2D: NA	ML and DL hybrid network for classification and prognosis [157]	ResNet18 with Gradient Boosting [157]	ACC: [157] AUC: [157]
SoT-5	[158, 159]	CT: [158] X-ray: NA LUS: [158]	3D:NA 2D: [158, 159]	Pleural line identification using ML [158], automatic severity assessment and exploration of severity related features using ML [159]	Hidden Markov Model and Viterbi Algorithm combined with SVM [158], Random forest [159]	ACC: [158, 159] AUC: [159] Sensitivity: [158] Specificity: [158] Others: [158, 159]
SoT-6	[160, 172]	CT X-ray: [160, 172] LUS:	3D:NA 2D: [160, 172]	Ensemble of DL and TL [160], multi-dilation CNN for extraction of COVID-19 features [172]	Custom CNN [160, 172], (VGG16, VGG19, Inception-V3, Xception, InceptionResNet- V2, MobileNet- V2, DenseNet201, NasNet-mobile) [160]	ACC: [160, 172] AUC: [160, 172] Sensitivity: [160, 172] Specificity: [160, 172] Others: [160, 172]
SoT-7	[161–165, 175]	CT:[165] X-ray: [163–165, 175] LUS: [161]	3D:NA 2D: [161–165, 175]	Explainable DL to provide explainability about the prediction [175], real-time internet based COVID-19 detection service [161], TL model trained on ensemble of two publicly available datasets [163], interpretable AI framework for COVID-19 classification [164], applying TL on comprehensive custom COVID- 19 CT and x-ray datasets [165]	VGG-16 [161, 175], Alexnet [165] DenseNet201 [162], Xception [163], InceptionNetV3 [164]	ACC: [161–165, 175] AUC: [161, 162, 164] Sensitivity: [161–165, 175] Specificity: [161–165, 175] Others: [161–164, 175]

design, allowing for a more nuanced classification. In our previous studies, we have also employed the concept of SoT. It is important to note that while the SoT aligns with the generations of architecture, it provides a more nuanced understanding of the differences between them.

The AI models used in different SoT along with their salient features are listed below.

SoT-1 represents an effective approach for quantifying the severity of COVID-19 lung damage and classifying the lung based on binary or multiclass frameworks. In this approach, lung segmentation is automated without the need for human intervention. This can be achieved using commercial software like XMedCon [179] or AI techniques such as threshold segmentation [180] or UNet-based segmentation [146]. The AI component in SoT-1 utilizes state-of-the-art or custom DL architectures.

SoT-2 serves a similar purpose as SoT-1, aiming to provide quantitative and categorical assessments of COVID-19 severity. However, it utilizes a more complex hybrid architecture compared to SoT-1. By integrating more than one AI architecture, including both DL and ML techniques, SoT-2 has exhibited comparable accuracy and the capability to accomplish supplementary sub-goals, including prognosis analysis. One drawback of SoT-2 is the increased effort and time needed to combine and fine-tune the different components of the AI.

SoT-3 is specifically designed to classify patients into different categories, such as non-COVID-19, COVID-19, and other types of pneumonia. Many COVID-19 studies utilizing AI have adopted SoT-3 for this purpose. Like SoT-1, SoT-3 automates lung segmentation. It employs an end-to-end automated pipeline that focuses on classifying pneumonia cases, including COVID-19. This approach enables faster and more straightforward implementation of research. However, one drawback of SoT-3 is its limited capacity to provide actionable insights for healthcare professionals in the treatment of patients suffering from COVID-19. For instance, SoT-3 does not facilitate the measurement of biomarkers that could indicate disease severity.

SoT-4 is centred around semi-automatic lung segmentation conducted by experts before the AI-driven processing of radiography images. It incorporates a hybrid AI component that combines different AI architectures to calculate multiple metrics. SoT-4 provides researchers with the flexibility to construct a pipeline that attains the desired balance between accuracy, complexity, and speed, depending on the specific metrics of interest. Nevertheless, a drawback of SoT-4 is the significant time required for designing the semi-automatic lung segmentation process and developing appropriate hybrid models.

SoT-5 involves the use of automated lung segmentation along with feature selection methods, manual feature engineering, and traditional ML models. The computed features are employed to calculate biomarkers, which are subsequently utilized for predicting the severity of COVID-19 and classifying patients. SoT-6 research utilizes a hybrid model for automated segmentation that combines DL and TL to generate categorical metrics for patient classification [181]. Similarly, SoT-7 research focuses on TL and comprises both an online and an offline system. In the

offline system, researchers manually extract relevant features from radiography images, which are then used to train a classifier. The trained coefficients are subsequently transferred to the online classifier, enabling real-time classification and prediction of COVID-19 severity. Effective lung segmentation using ML techniques has been demonstrated in previous studies [146, 167]. Figure 2.8 showcases an online ML-based COVID-19 risk prediction system, which is consistent with the ML systems previously published by the research group [165, 182, 183].

Figure 2.9 displays a DL architecture reference, established using [184]. Among various DL architectures, the convolutional neural network (CNN) is extensively employed. CNNs employ multiple convolutional filters to extract basic visual features from input image data. These filters are stacked in layers to capture more complex visual features. Pooling layers are frequently integrated with CNN layers to reduce spatial information in the intermediate representation, while padding layers help preserve the correct data dimensions.

TL is an advanced technique that enhances the capabilities of DL architectures. It involves pre-training these architectures on large datasets, enabling them to achieve

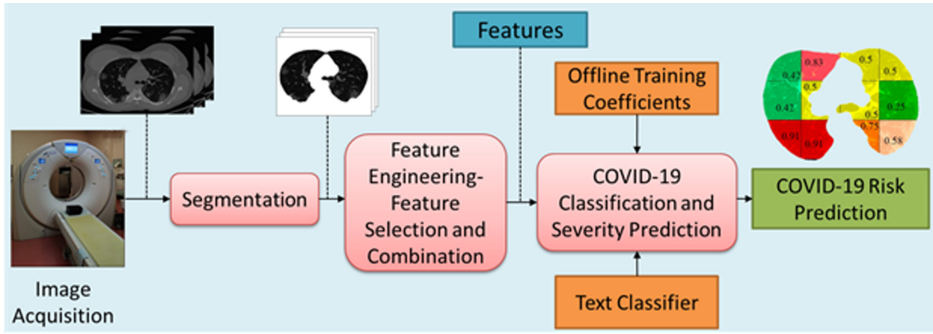

Figure 2.8. An online ML-based COVID-19 risk prediction system. (Courtesy of AtheroPoint™, Roseville, CA, USA; reproduced with permission).

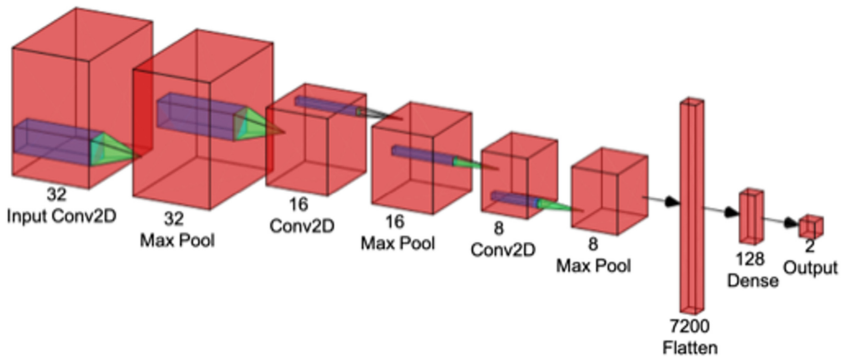

Figure 2.9. A custom CNN-based DL architecture comprising different layers.

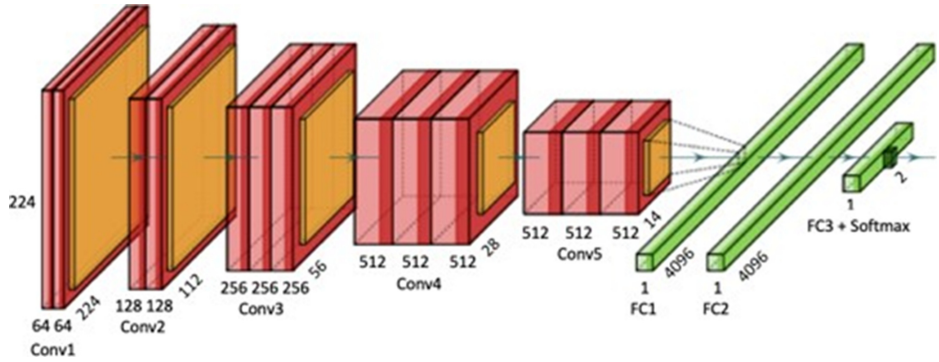

Figure 2.10. An example of transfer learning (TL) architecture using VGG16.

higher accuracy even with limited training data, less powerful hardware, or restricted training time. The reference architecture for TL, called VGG16, is depicted in figure 2.10, as described in [185].

Table 2.3 gives us a comparative analysis of multi-modal AI architectures that are utilized for the diagnosis of COVID-19, highlighting their main characteristics. The 'Arch Type' column provides reference to seven different architectures developed according to the workflow and goals of various AI research studies. The 'Reference' and 'Modality' attributes indicate the sources referenced and the specific imaging modality employed. The attribute '3D/2D Imaging' indicates that the research is either focused on three-dimensional or two-dimensional radiological imaging, as discussed in [186, 187].

The attribute 'Highlight/Objective' in the table signifies the distinctive aspect or objective that the research might have. The 'Architecture Description' attribute provides a description of the specific AI architecture utilized in the study. The 'Performance Metrics' attribute indicates the metrics employed by the researchers to assess the effectiveness of their work. For a more in-depth understanding of AI and the applications, readers are advised to explore specialized reviews that focus on AI-based methodologies.

2.6 Workflow considerations for COVID-19 lung characterization: CT vs. x-ray

The three chest-imaging modalities x-ray, CT, and ultrasound have been strongly recommended by WHO for the diagnosis of COVID-19 [90]. In their guidelines, the following observations were given for COVID-19 diagnosis. (i) x-rays was found to be lower in sensitivity and higher specificity than chest CT imaging [188, 189]. (ii) Chest x-rays are less expensive, have lower radiation, take less acquisition time, and are less expensive to use for monitoring than CT. (iii) Chest CT was found to have higher sensitivity but lower specificity and emits more radiation than x-ray. (iv) Lung ultrasound was found to have very low diagnostic accuracy but offers an alternative for several other applications, such as the abdomen, carotid, urology, obstetrics, and gynaecology imaging. On the other hand, ultrasound has a high risk

of COVID-19 infection transmission due to close contact with the patient compared to other imaging modalities. In accordance with the guidelines published by the American College of Radiology on April 8, 2020 [190], MRI is not recommended for COVID-19 patients due to the elevated risk of infection [91]. While there are studies available on MRI and COVID-19 [92–94], no specific literature was found that directly addresses the combination of COVID-19, MRI, and AI. The main reason is the long scanning time, risk of infection, and high cost associated with MRI. On the contrary, FDG-PET/CT imaging, which is a more advanced technique compared to CT alone [191], has been used in many studies for diagnosing COVID-19 [95, 96]. However, no relevant studies combining FDG-PET/CT imaging, COVID-19, and AI were found. This could be attributed to the higher cost associated with PET/CT imaging [23, 192].

X-ray and CT imaging modalities are considered appropriate for COVID-19 diagnosis according to the recommendations of the World Health Organization, as indicated in table 2.4. Figure 2.11(c) demonstrates the percentages of studies utilizing either CT, x-ray, or both modalities, with CT being regarded as the gold standard. Several significant studies have been conducted using AI for automated COVID-19 diagnosis with x-rays and CT [21–23, 192–202]. Open-source COVID-19 datasets for x-ray and CT imaging, such as the one provided by RSNA, have gained popularity in the scientific community.

To compare studies involving x-ray and CT imaging, several attributes were considered, including the risk classes, number of subjects, 2D vs. 3D imaging, AI models, automated vs. non-automated ROI segmentation, augmented vs. non-augmented techniques, hardware and software used, K-fold cross-validation, performance, and optimal models. Several notable studies [203–208] included cohorts of over 1000 subjects. The number of classes in the studies was categorized into multiclass and binary classifications, with a majority focusing on binary classification [203, 204, 209–216]. While most studies utilized 2D x-ray images, two studies employed 3D CT volumes as input [210, 212]. ROI segmentation, an essential step in chest image analysis, was mostly automated, with five studies

Table 2.4. Compatibility of imaging modality for COVID-19 and adaptability for AI [230]

Imaging modality	Suitable for COVID-19 as per WHO guidelines	Cost	Risk of radiation	Risk of infection due to close contact	Compatible with AI for COVID-19 diagnosis
PET/CT	High	Very high	Very high	Low	Low
CT	High	High	Very high	Low	Very high
X-ray	Medium	Low	High	Low	Medium
Ultrasound	Low	Low	No	High	Low
MRI	Low	High	No	Low	Low

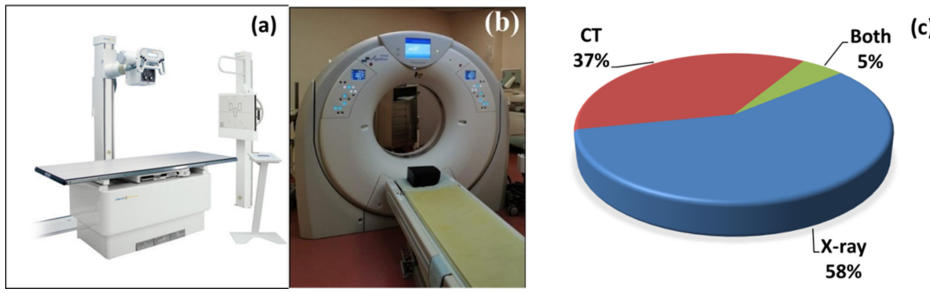

Figure 2.11. (a) An x-ray scanner. (b) A CT-scanner (Courtesy of Luca Saba, University of Cagliari, Italy). (c) Studies using CT vs. x-ray.

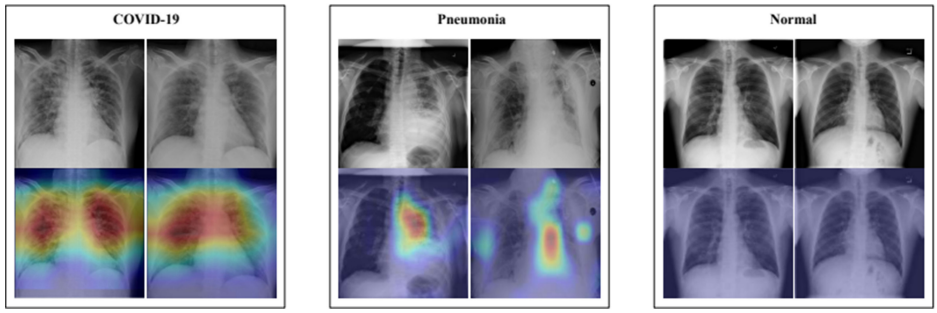

Figure 2.12. X-ray scans of COVID-19, pneumonia, and normal lungs [219] (permission pending).

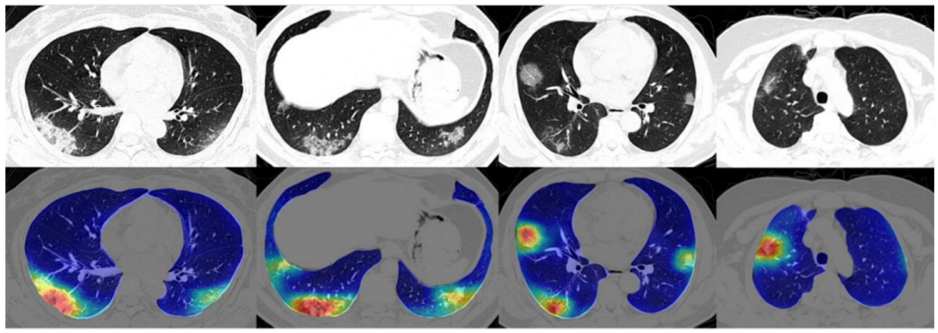

Figure 2.13. CT scans classified as positive for coronavirus abnormalities and their corresponding color heatmaps [220] (permission pending).

employing automated methods [203, 211, 212, 217, 218], and one study using manual segmentation [209]. Full-sized images were predominantly utilized in the classification process.

Regarding AI models, the studies primarily fell into two categories: ML and DL. In one study, a network based on DL achieved a classification accuracy of 90.13% when distinguishing pneumonia, normal, other diseases, and COVID-19 cases in chest x-rays [219]. Figure 2.12 visualizes sample images and their corresponding

colour maps from this study. Another study utilized a network based on DL to detect COVID-19 abnormalities in lung CT scans and generate a heatmap indicating severity levels [220]. Figure 2.13 provides an illustration of the resulting images.

To address data limitations in medical studies, image augmentation techniques were commonly employed. Transfer learning with DL models was particularly utilized when datasets were small, often consisting of a few thousand samples [210–212, 215, 218]. These augmentation techniques involved various operations such as image transformation, blurring, and colour manipulation. Some studies also adopted a patch-based framework with a small number of trainable parameters, incorporating multi-scaling for spatial features in diagnosis of COVID-19 [221, 222]. Cross-validation, specifically the K-fold strategy, was frequently used to evaluate AI performance. Authors employed five-fold [203, 205, 215, 218], and ten-fold [207] cross-validation approaches to comprehensively assess model performance.

To prevent overfitting during AI model optimization, researchers utilized techniques like cross-validation and transfer learning in supervised learning. Overfitting occurs when a model performs well on known data but struggles with unknown data. Increasing the training dataset size was among the approaches used to mitigate overfitting. The performance of the classifier was influenced by various factors, including the training iterations, number of subjects, training time, and sample size. At present, there is no definitive best-performing model or method that can be identified. However, as further trials and studies are conducted, it is anticipated that superior AI models will be emerging.

2.7 Critical discussion

Clinical requirements for COVID-19 AI systems. To develop an optimal AI system for COVID-19, it is crucial to meet several key clinical requirements. Firstly, the system should demonstrate robustness and stability, ensuring that its output remains reliable and consistent even in the face of variations in patient demographics or other related characteristics. Secondly, it should demonstrate reliability and reprehensibility, consistently producing results that are similar in multiple trials. In addition, when deployed in an operating room, the AI system should be cost-effective and have reasonable speed compared to traditional techniques for diagnosing COVID-19, like RT-PCR tests. To ensure broad applicability, the AI system should be trained and tested on a diverse and representative dataset, ensuring its generalization. It is essential for the AI system to provide an accurate assessment of COVID-19 severity, as this metric plays a critical role in guiding treatment decisions for patients. Incorporating this capability into an AI diagnostic system is highly desirable. Overall, an ideal system embedded with AI for COVID-19 must meet these clinical requirements to effectively assist healthcare professionals in diagnosing and managing the disease.

Validation of the AI system's results by radiologists, pulmonologists, and doctors is necessary to assess its effectiveness. Furthermore, the AI system should utilize 3D imaging to segment and analyze the impact of COVID-19 on various organs, providing additional support to clinicians. By integrating these clinical

requirements, there is significant potential for enhancing the current state of AI-assisted diagnostics for patients suffering from COVID-19. This has the potential to greatly improve the current standard of care by incorporating AI technology into the diagnostic process.

System optimization. DL techniques are extensively utilized in DL-based AI systems for the detection and classification of COVID-19. Researchers have employed data augmentation techniques to increase the size of the training dataset for COVID-19. The choice of the number of convolution layers in DL models is typically based on researchers' intuition. However, it is crucial to optimize DL-based AI systems for COVID-19 by considering the relationship between augmentation, the resulting classification accuracy, and the number of convolution layers. This optimization process can lead to enhanced performance and accuracy in COVID-19 classification tasks. Please refer to figure 2.14 for a visual representation of these concepts.

Scientific validation. To validate and evaluate an AI-based COVID-19 diagnostics system, it is essential to consider a wide range of comorbidity conditions. Various scenarios should be taken into account where assumptions may differ. For instance, modifying the thickness of CT scans or providing different views (coronal, sagittal, axial) to the system for the purpose of diagnosing can impact its performance. Moreover, the validation of system stability must be done by altering the combination of data used and employing partition protocols like K10, K5, and K2. A AI system which is stable will demonstrate minimal standard deviation across different data combinations [165]. Additionally, the system should undergo validation using patients from diverse age groups and with different comorbidities to ensure its robustness and reliability in real-world applications. These validations have great importance in establishing effectiveness and generalizability of the AI-based diagnostics systems that are used for COVID-19 [165].

Clinical validation. To gain approval from regulatory authorities, it is vital to conduct gold standard validation for the research. This involves comparing the predictions made by the AI system with a physical examination of the body's organs. One method to accomplish this is to validate the body tissues

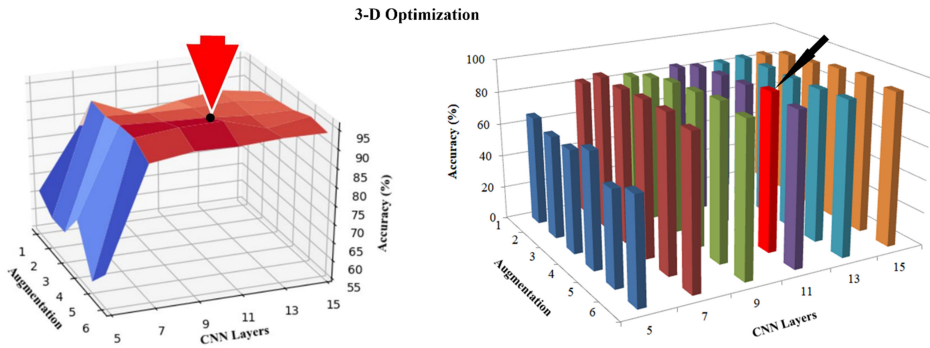

Figure 2.14. A 3D graph representing the relationship between CNN layers, data augmentation, and accuracy. (Courtesy of AtheroPoint™, Roseville, CA, USA; reproduced with permission [14].)

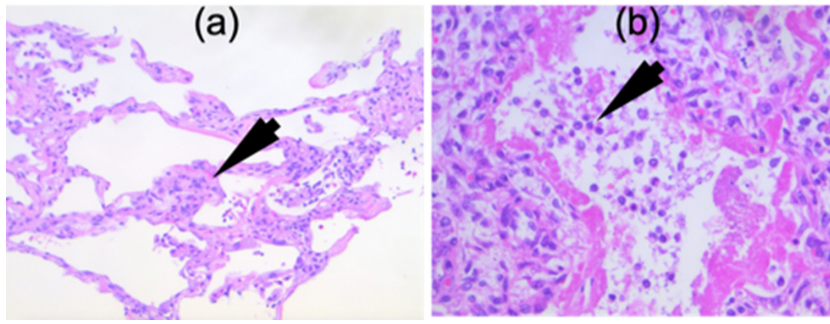

Figure 2.15. Microscopic views of (a) interstitial pneumonia and (b) COVID-19 pneumonia. (Courtesy of Luca Saba, A.O.U., Cagliari, Italy.)

microscopically to evaluate how severe the ARDS is which has resulted from COVID-19, as shown in figure 2.15. Furthermore, it is crucial to perform an analysis of intra-observer and inter-observer variability [223] to address any potential human bias in the system. These validations play a critical role in ensuring the accuracy and reliability of the AI system's predictions, thereby increasing its credibility and acceptance by regulatory authorities [223].

AI for COVID-19 comorbidity and age-group frameworks. The AI system's design should be flexible enough to consider patients' comorbidities, including conditions such as cardiovascular diseases, diabetes, obesity, pancreatic diseases, retinopathy, angiography, and blood vessel diseases [224], with their corresponding age groups. In [225], a study was conducted to develop an AI system for predicting cardiovascular diseases in a diverse patient population. Similarly, the AI systems discussed in [226, 227] can be extended to incorporate comorbidities and different age groups to enhance the accuracy of COVID-19 diagnosis.

To address this challenge, the primary AI system can be divided into multiple subsystems, each tailored for specific comorbidity categories and further categorized based on different age groups. For example, if there are five comorbidities and three age groups, a total of 15 subsystems would be developed. Each subsystem should be trained independently using a distinct gold standard database [228]. By incorporating additional input data related to the patient's comorbidities and age group, an appropriate AI subsystem can be identified for each new patient.

3D image acquisition and processing. The majority of AI research on COVID-19 has predominantly focused on evaluating the severity of lung infection using 2D imaging, which may not fully capture the disease's progression. To overcome this limitation, there is a need to explore COVID-19 data in 3D, as depicted in figure 2.16. One potential approach is to utilize scans acquired during the contrast enhancement of a lung ultrasound, which can provide valuable insights for early management and prognosis of COVID-19 [231]. In a study cited in [232], researchers employed 3D CT scans to diagnose and classify lung lesions affected by COVID-19, offering a more comprehensive understanding of the disease's characteristics. Furthermore, in another study mentioned in [233], the authors utilized the

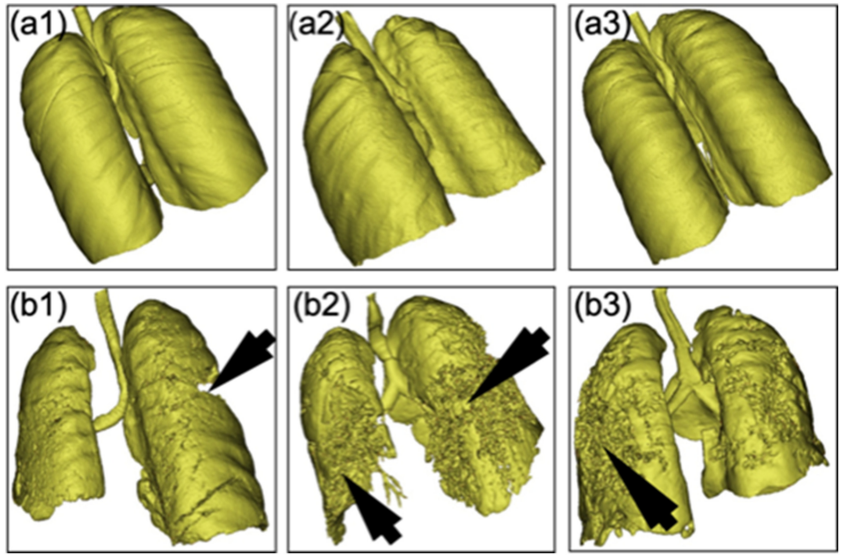

Figure 2.16. Three lungs with non-COVID-19 pneumonia (a1, a2, and a3). Three lungs with COVID-19 pneumonia with different COVID-19 severities (b1, b2, and b3). (Courtesy of AtheroPoint™, Roseville, CA, USA; reproduced with permission.)

DensNet121-FPN architecture and a deep learning strategy for lung segmentation and classification, leading to improved accuracy in the analysis.

Multi-modality data. Radiographic techniques provide several diagnostic options for COVID-19, including lung chest x-rays, CT, PET/CT scans, and lung ultrasound. The choice of the appropriate imaging modality depends on factors such as the patient's age, pre-test probabilities (PTPs), and comorbidities [18]. To evaluate the severity of a COVID-19 infection, troponin levels can be used as a PTP test, serving as an indirect indicator of hypoxia. In the early stages of COVID-19, x-rays and lung ultrasounds are cost-effective and easily accessible diagnostic tools, given their compact size. However, for patients with comorbidities, advanced age, or COVID-19-induced acute respiratory distress syndrome (ARDS) leading to hypoxia, lung CT is often the preferred choice. Lung CT provides robust diagnostic capabilities and higher resolution in such scenarios. When developing systems embedded with AI for COVID-19, it is crucial to ensure their adaptability and generalizability across multiple imaging modalities to cater to the specific needs of individual patients. By considering these factors and the insights presented in the cited references, AI systems can be effectively designed to integrate and analyze data from different imaging modalities, thereby optimizing the diagnostic process for COVID-19 patients.

Tissue characterization of lung scans. In one of the last investigations [3], an analysis was conducted using bispectrum (B) on lung tissues affected by COVID-19. The study employed a higher-order spectrum (HoS) approach which validated the

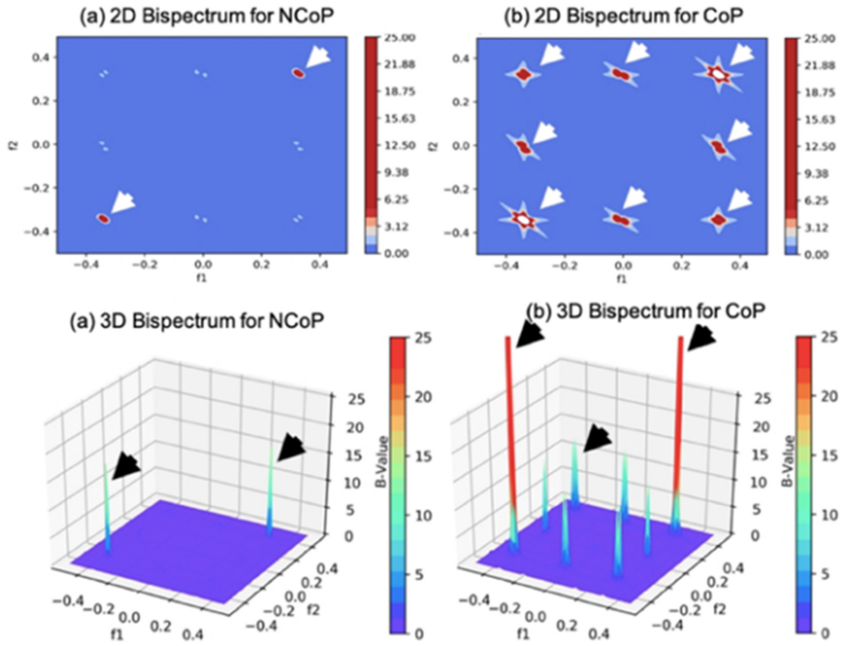

Figure 2.17. Bispectrum analysis of non-COVID-19 pneumonia (NCoP) and COVID-19 pneumonia (CoP). (Courtesy of AtheroPoint™, Roseville, CA, USA; reproduced with permission.)

findings and was not dependent upon the AI for any validation. The results, illustrated in figure 2.17, revealed that samples infected by COVID-19 exhibited significantly higher B-values compared to non-infected samples. This observation suggests that AI systems can effectively utilize these patterns to differentiate between non-COVID-19 and COVID-19 samples. By incorporating such insights and methodologies, AI systems can enhance their capability to accurately identify and distinguish cases of COVID-19.

Data collection. To mitigate biases related to ethnicity, comorbidity, age, and other factors among COVID-19 patients, it is highly advantageous to collect data over an extended period and from diverse geographical locations [234]. This approach ensures the inclusion of a more representative and comprehensive dataset. Furthermore, the patient data should encompass multiple classes, including a control group and various types of pneumonia classes such as HIV, viral, COVID-19, MERS, and bacterial [235]. By adhering to these criteria, the development of a more robust and generalized AI system for COVID-19 diagnostics becomes feasible, eliminating the need for localized validations or retraining. Such an approach facilitates the creation of a versatile solution that accounts for the inherent variations and complexities in different patient populations. By considering these aspects, AI systems can be designed to deliver accurate and reliable COVID-19 diagnostics, benefiting healthcare providers worldwide.

AI and hardware constraints. GPUs have a vital role in DL investigations, providing the necessary computational power for both training and testing phases [234, 235]. Researchers heavily depend on GPUs for their computational capabilities. Popular open-source platforms like Google Colab are frequently used, with Python being the programming language of choice, along with frameworks like TensorFlow or PyTorch [14, 102].

Strengths, limitations, and extensions. This research offers important findings on different aspects of ARDS in relation to comorbidity, medical imaging modalities for COVID-19 patients with ARDS, workflow considerations for imaging tools, AI architecture design for diagnosing the severity of ARDS-related lung conditions, and the role of AI in managing comorbidities. The research emphasizes the essential elements required for a dependable and secure AI-driven approach to evaluate the severity of COVID-19.

Although this study introduces novel approaches by incorporating AI designs based on comorbidity, it acknowledges that there are other aspects that could be included for a more comprehensive analysis. For example, further exploration of the biological processes underlying comorbidities could provide valuable insights, but due to limitations in the length of the manuscript, they were not included. Additionally, more rigorous comparisons of deep learning paradigms could be incorporated, and the study references previous dedicated reviews that offer opportunities for further exploration in these areas (table 2.5 and 2.6).

Future research should focus on developing methods that utilize GPS within targeted lung regions in 3D and 2D medical images for rapid assessment of COVID-19 severity. These methods should take into account factors such as comorbidity and time constraints to enable accurate and timely determination of severity [236–238]. Additionally, this foundational study creates opportunities for further exploration in various medical fields, including cardiology, neurology [239], ophthalmology [241], and diabetology [240]. The application of statistical tools, such as systematic review and meta-analysis (SRMA), can provide comprehensive and evidence-based insights in these areas. However, it is important to note that the inclusion of SRMA goes beyond the current scope of this narrative review.

2.8 Conclusion

This recent study focuses on the investigation of various comorbidities, their impact on an ARDS-based framework, and their association with mortality rates. The study proposes solutions based on AI that incorporate comorbidity as a factor that is independent in the design. It presents the key features and architectural characteristics of seven different SoT approaches. The study highlights the need for a thorough investigation of AI system's important components before its clinical application for diagnosing severity of COVID-19. These components include clinical and scientific validation, optimizing the architecture design by balancing layers and augmentation, and selecting the appropriate imaging modality based on the troponin release and severity of COVID-19 symptoms. The study concludes that the incorporation of comorbidity and age group as novel features in AI design holds great promise for characterizing ARDS in the future [242–245].

Table 2.5. Artificial Intelligence-based studies for automatic COVID-19 detection using lung CT.

SN	References	#Subj.	Risk Class	2D vs. 3D	*ROI	AI Model	Augm.	CV	H/W-S/W	Optimal model	Performances
1	Ardakani *et al* (2020) [209]	194	2	2D	×	CNN+TL	×	NA	SPSS software (version 24, IBM)	ResNet101	ACC:99.51% SE:100% SP:99.02% AUC:0.994
2	Wu *et al* (2020) [217]	495	3	2D	✓	CNN+TL	×	NA	GPU Python	ResNet50	ACC:76.0% SE:81.1% SP:61.5% AUC:0.819
3	Zheng *et al* (2020) [210]	499	2	3D	×	3D CNN+TL	✓	NA	GPU PyTorch	UNet	ACC: 90.1% SE: 90.7% SP: 911% AUC: 0.976
4	Yang *et al* (2020) [211]	679	2	2D	✓	CNN	✓	NA	GPU PyTorch	DenseNet169	ACC:89% FS :90% AUC:0.98
5	Gozes *et al* (2020) [212]	270	2	2D and 3D	✓	3D + 2D CNN	✓	NA	NA	ResNet50	SE: 98.2% SP: 92.2% AUC: 0.996

(*Continued*)

Table 2.5. (*Continued*)

SN	References	#Subj.	Risk Class	2D vs. 3D	*ROI	AI Model	Augm.	CV	H/W-S/W	Optimal model	Performances
6	Shi *et al* (2020) [203]	2685	2	2D	✓	ML (RF)	×	K5	NA	RF	ACC:87.9% SE: 90.7% SP: 83.3% AUC: 0.942
7	Liu *et al* (2020) [213]	746	2	2D	×	LA-DNN+ TL	×	NA	NA	LA-DNN	ACC:88.8% F1S: 94.7% AUC: 0.88
8	Panwar *et al* (2020) [204]	2482	2	2D	×	CNN+TL	×	NA	NA	VGG19	ACC:87.9% SE: 90.7% SP: 83.3% AUC: 0.942

#Subj.: Number of subjects in the study; Augm.: Augmentation; NA: Not available; ACC: Accuracy, SE: Sensitivity; SP: Specificity; AUC: Area under the curve; F-M: F-measure; KP: Kappa statistics; TL: Transfer Learning; FS: F1-Score LA-DNN: lesion-attention deep neural network; RF: Random forest; ML: machine learning; H/W: Hardware; S/W: Software; CV: Cross-Validation; K5: five-fold; ROI: Automated Region of Interest.

Table 2.6. Artificial Intelligence-based studies for automatic COVID-19 detection using lung x-ray.

SN	Reference	#Subj.	Risk Class	2D vs. 3D	Auto ROI	AI Model	Augm.	CV	H/W-S/W	Optimal Model	Performances
1	Narayan Das *et al* (2020) [216]	NA	3	2D	×	CNN+TL	×	NA	NA	Proposed CNN	ACC: 97% FM: 96% SE: 97% SP:97% KP:0.97
2	Ouchicha *et al* (2020) [205]	2905	3	2D	×	CNN	×	K5	NA	CVDNet (proposed CNN)	ACC: 90% PR: 96.72% RC: 96.84% FS: 96.68%
3	Hemdan *et al* (2020) [214]	50	2	2D	×	CNN	×	NA	GPU Python	VGG19 DenseNet201	ACC: 96.69% PR: 83% RC: 100% FS: 91%
4	Zhang *et al* (2020) [215]	43 370	1, 2	2D	×	CNN	✓	K5	NA	CAAD (proposed CNN)	ACC: 78.57% SE: 71.70% SP:79.40% AUC: 0.83
5	Togacar *et al* (2020) [218]	458	3	2D	✓	CNN+TL	✓	K5	CPU MATLAB	MobileNet-V2	ACC: 99.24% SE: 100% SP: 97.72% FS: 99.43%

(*Continued*)

Table 2.6. (*Continued*)

SN	Reference	#Subj.	Risk Class	2D vs. 3D	Auto ROI	AI Model	Augm.	CV	H/W-S/W	Optimal Model	Performances
6	Farooq *et al* (2020) [206]	2839	4	2D	×	CNN+TL	✓	NA	NA	ResNet50	ACC: 96.23% RC: 100% PR: 100% FS: 100%
7	Cozzi *et al* (2020) [207]	1427	3	2D	×	CNN+TL	×	K10	NA	VGG19	ACC: 96.78% SE: 98.66% SP: 96.46%
8	Pereira *et al* (2020) [208]	1144	7	2D	×	ML+DL+TL	×	NA	NA	Multilayer Perceptron	FS: 89%

#Subj.: Number of subjects in the study; Augm: Augmentation; NA: Not available; ACC: Accuracy; SE: Sensitivity; SP: Specificity; AUC: Area under the curve; F-M: F-measure; KP: Kappa statistics; PR: precision; RC: recall; FS:F-Score; TL: Transfer Learning; LA-DNN: lesion-attention deep neural network; ML: machine learning; H/W: Hardware; S/W: Software; CAAD: confidence-aware anomaly detection model; ROI: Region of Interest.

Symbol table

SN	Acronyms	Description
1	2D	Two dimensions
2	3D	Three dimensions
3	ACC	Accuracy
4	AI	Artificial intelligence
5	ARDS	Acute respiratory distress syndrome
6	AUC	Area-under-the-curve
7	CNN	Convolution neural network
8	CT	Computed tomography
9	DL	Deep learning
10	FS	F1-score
11	GPU	Graphics Processing Unit
12	H/W and S/W	Hardware and software
13	LUS	Lung ultrasound
14	ML	Machine learning
15	MRI	Magnetic resonance imaging
16	RF	Random forest
17	RSNA	Radiological Society of North America
18	SE	Sensitivity
19	SP	Specificity
20	TL	Transfer learning
21	US	Ultrasound
22	X-ray	Röntgen radiation

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