

Artificial Intelligence in Echocardiography and Cardiac POCUS (Point-of-Care-Ultrasound) during the COVID-19 Pandemic: A New Paradigm?

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ABSTRACT

Echocardiography and cardiac point-of-care-ultrasound (POCUS) have become invaluable tools in the diagnosis and management of several cardiovascular complications associated with COVID-19. These diagnostic procedures provide physicians with a real-time visualization of cardiac anatomy and function, allowing them to quickly and accurately identify abnormalities that may arise because of the viral infection. The COVID-19 pandemic has triggered major changes in clinical practice worldwide, requiring modern medicine to embrace a new approach to health care, the use of new technologies and clinical tools. Time constraints and physician safety issues inherent in the initial assessment of cardiovascular complications due to COVID-19 have established considerable challenges for healthcare professionals across the globe. The advent of artificial intelligence (AI) has been a game-changing tool in medicine as it is a powerful asset that has expanded the arsenal of modern clinicians and helps them improve the accuracy and safety of clinical assessment. In this review, we scrutinize different AI-based analyses of echocardiography and cardiac POCUS, which are pivotal tools for the diagnosis of cardiovascular complications related to COVID-19. Many hospitals have extensively used AI to improve patient care and ensure physician safety in the midst of the pandemic, which emphasizes the critical role of artificial intelligence in comprehensive healthcare delivery.

Abbreviations: POCUS: Point-of-Care-Ultrasound; COVID-19: Coronavirus Disease-19; ML: Machine learning; AI: Artificial Intelligence; US: Ultrasound; ATLS: Advanced Trauma Life Support; 3D: Third Dimension; RT: Reverse Transcription; GLS: Global Longitudinal Strain; LV: Left Ventricular; LVFF: Left Ventricular Ejection Fraction; EF: Ejection Fraction; CVC: Central Venous Catheter; AMC: Associative Memory Classifier

Introduction & Background

Since the beginning of the coronavirus disease-19 (COVID-19) pandemic in Wuhan, China several technological developments have had to be enhanced to adapt to our new reality. The use of artificial intelligence (AI) has had significant development in recent years with widespread applications being used in medicine [1]. Consequently, the implementation of AI for the identification, classification, and di-

agnosis of echocardiographic images during the pandemic grew exponentially in medical centers around the world [2]. Moreover, cardiac point-of-care-ultrasound (POCUS) is a type of echocardiographic assessment that guides a clinician in the initial evaluation and management of select patients. Its continuous use since it was first described in the 1990s, prompted a useful tool that has aided in the management of the complex COVID-19 patient with cardiovascular complications.

However, both echocardiography and POCUS are operator-dependent and in inexperienced hands, they may skew the appropriate diagnostic assessment [1]. The use of AI in cardiac imaging has reduced the risk of misdiagnosis in certain cases and has proven especially useful in COVID-19 due to reduced exposure to the virus. This review will help researchers and clinicians expand on the current utility of AI in cardiac imaging during the COVID-19 pandemic.

Artificial Intelligence in Medicine

AI in medicine refers to the utilization of software to aid human cognition in the analyzing, presenting, and comprehending complex medical data [1,2]. AI comprises computer tools that replicate human intelligence processes including, learning, reasoning, and self-correction [1,2]. Through various algorithms, machines learn and can make decisions [2]. However, nowadays it is difficult to establish a universal definition to what is known as AI. The term itself is often applied to the field of computer science, which endeavors to mimic human cognitive processes, learning capacity, knowledge, memory storage, and improvement through trial and error [1-7]. The term AI was first used in the 1950s [2-4]. It emerged to name computer systems that emulated certain processes of the human mind. However, early models faced several limitations, hindering widespread acceptance and application in medicine [2,3]. In the 1970s, the first experience in the health sector was shared with a new software called Mycin [4]. This system was aimed to detect infectious blood diseases and communicate with users in natural language. It also prescribed medications individually tethered to each patient [4]. This software is considered one of the most significant early uses of AI in medicine. Other systems such as INTERNIST-1 and CASNET were also employed in the early days of AI but were discontinued due to inaccurate results [4]. Furthermore, in the 1980s and 1990s, modern, high processing computers positively impacted medicine after microchips further improved automated software [5].

The advances in computer science prompted new levels of connectivity, and with the use of worldwide networks, exponentialize AI's advancement [5]. During this time, researchers and developers recognized that AI systems in healthcare must be designed to accommodate and improve data and aid, rather than replace, the expertise of clinicians [3-5]. Currently, these new technologies have allowed the growth of AI applications in healthcare [2-6]. Faster collection and processing capacity of clinical data, improvements in computer vision processing time, have allowed machines to replicate human perceptual processes exponentially. High-specificity robot-assisted surgery,

better insight and data records on rare diseases, electronic medical record systems, increasing knowledge in the genomic sequencing, and software that recognizes pathological abnormalities during medical procedures have already successfully applied this type of robotic intelligence [2-7]. The applications of AI in medicine are based on several principles, such as improving accurate diagnosis and treatment, utilizing of robotic tools, relieving the burden on doctors, and drug development [5-7]. Nowadays, there is virtually no branch of medicine that does not actively research AI to enhance diagnostic and therapeutic methods. In Radiology and Infectious diseases, more accurate and detailed methods through computerized tomography and magnetic resonance imaging have been developed, significantly improving the diagnostic accuracy. In Oncology, there is ongoing research into the early detection of cancer and the identification of the most effective treatments. Likewise, in Cardiology, several groundbreaking applications have been developed [2-13].

Current Applications of Artificial Intelligence in Cardiology

Machine learning (ML) and deep learning, integral parts of AI, can assist healthcare providers in automating various tasks in echocardiography, serving as a valuable diagnostic tool [14] (Figure 1). It can help expand research capabilities and discover alternative paths in medical management in an automated manner pre-established by a software [14] (Figure 2). Moreover, several advances have already been made to implement fully automatic interpretation of echocardiographic images [15]. This has been accomplished through automated identification of views, image segmentation, quantification of structures and functions, as well as the detection of cardiac conditions [15]. One of the most developed applications of ML in Cardiology is the prediction of cardiac arrhythmias [16]. Numerous studies describe algorithmic models for atrial fibrillation development, using ML predictive systems composed of different threads: signal processing, extraction of significant variables, and classification algorithms [15]. Another application is the use of AI to identify phenotypes and classify hypertrophic cardiomyopathies [17]. Additionally, the software and algorithmic management of the ML system could help avoid hospitalizations for heart failure and recognize patients susceptible to cardiac decompensation after hospital discharge [15]. Studies have indicated that ML could improve the clinical outcomes of these patients [14]. Another noteworthy area is heart transplantation, with ML systems applied to predict the probability of death or the option of heart transplantation [14].

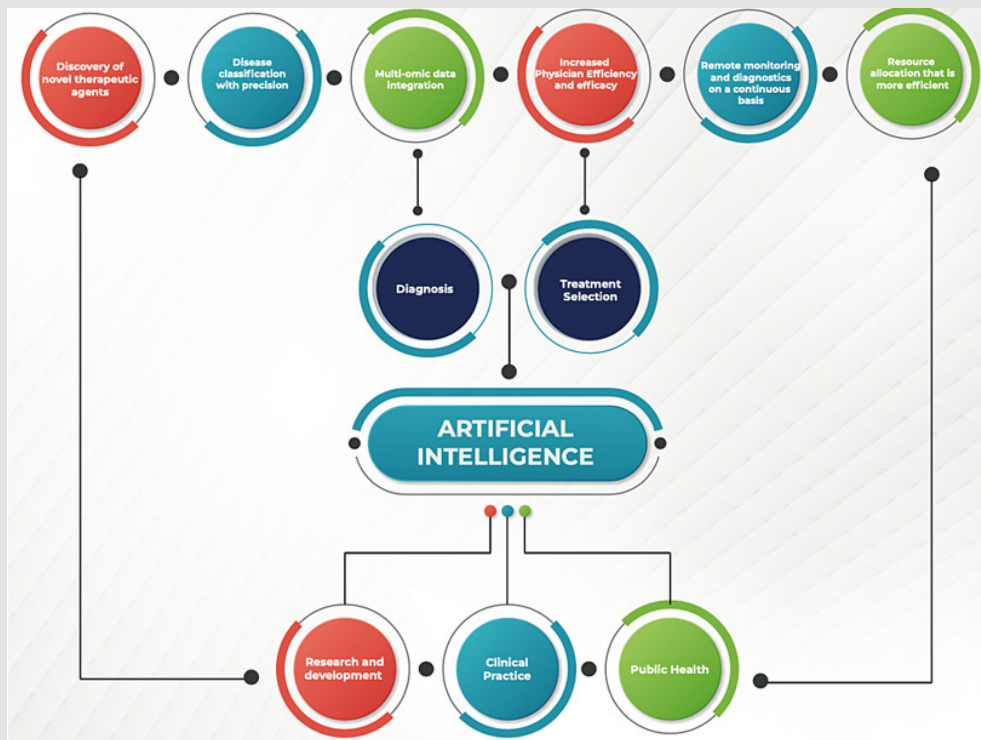


Figure 1: Applications of AI in Cardiology.

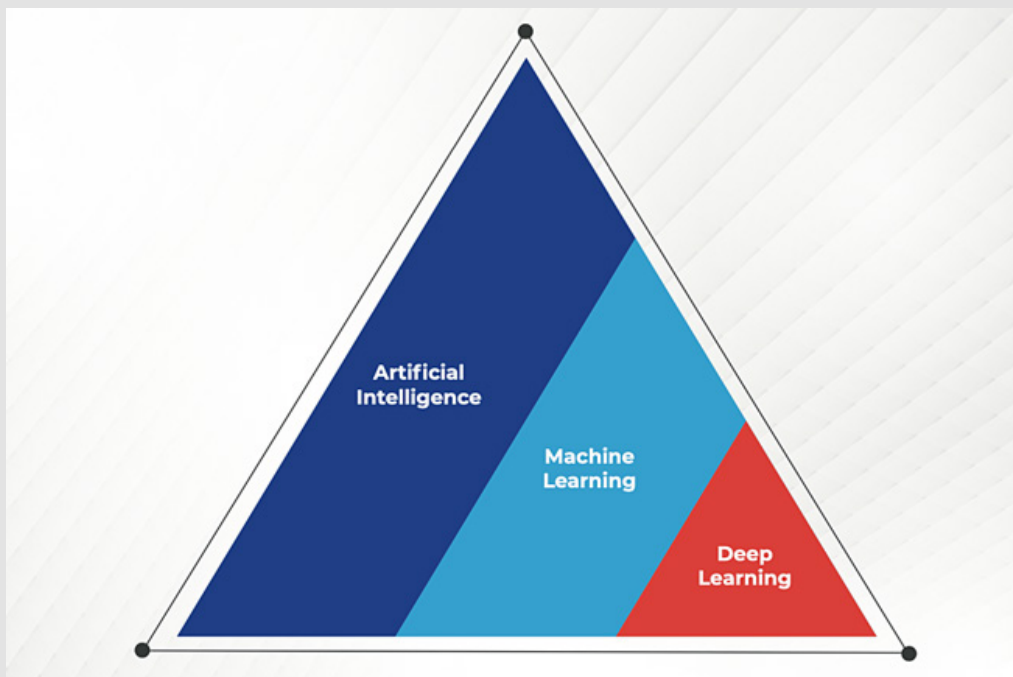


Figure 2: AI, ML and deep learning.

Basics of Ultrasound

Sound, as defined in physics, is mechanical energy that propagates through matter, taking advantage of its elastic properties [18,19]. It carries vibrational and longitudinal movements that spread parallel to the direction of the vibration [18,19]. Ultrasound (US) technology uses the aforementioned principles to generate images [19]. It produces high frequency sounds, imperceptible to the human ear, which are subsequently interpreted by a machine's algorithm to produce real-time images. Echocardiography employs US to assess the structural components of the heart [20]. Since the first recording of an echocardiogram in 1953 by Edler and Hertz, the technological advancements in echocardiography have profoundly influenced modern cardiology [20]. Point-of-Care Ultrasound (POCUS) echocardiography adopts a practical approach to obtain necessary images for clinical decisions in the least amount of time [21,22]. It is not as profound or detailed as an echocardiographic assessment performed by Cardiologists, but it provides sufficient information to make clinical decisions at the bedside [22]. Widely accepted since the 1990s, POCUS echocardiography has been embraced by numerous hospitals worldwide as a routine diagnostic measure [22].

Point-of-Care Ultrasound

POCUS is a diagnostic and procedural guidance ultrasound tool performed by a clinician during a patient encounter to help guide the evaluation and management of the patient [23]. It is an evolving outpatient, inpatient, and urgent care diagnostic tool which is performed and interpreted at the bedside [24]. Interest in POCUS has grown steadily over the last few decades since it provides immediate availability and real-time images that can guide medical decision making [25]. Frontline physicians, mostly surgeons, and emergency medicine physicians, began assessing trauma patients with ultrasound in the 1970s [25]. Following this trend, in the early 1990s, the term FAST exam, or Focused Assessment with Sonography in Trauma, was coined [25]. From its early description in the 1970s in Europe to its incorporation into (ATLS) guidelines in the 1990s in the United States, the FAST exam set a precedent for incorporation of POCUS into routine clinical practice [25]. Additionally, POCUS has been used to aid in the diagnosis of multiple medical conditions ranging from acute appendicitis, small bowel obstruction, heart failure, pericardial effusions, airway compromise, abdominal aortic aneurysm, traumatic injury assessment to COVID-19 [26-29]. Although the gold standard diagnostic test for COVID-19 is reverse transcription-PCR (RT-PCR), POCUS has proven to be a safe and quick first-line bedside diagnostic alternative for COVID-19 lung, cardiac, and thromboembolic manifestations [27,29].

In addition to disinfection being faster and easier and improved portability, POCUS is an invaluable first-line diagnostic tool for COVID-19 patients [27-29]. Because of its ease of use, it has emerged as a viable option in cases where a formal radiological study would cause a delay in diagnosis and/or treatment [29]. Additionally, COVID-19 undoubtedly causes several cardiovascular manifestations.

Acute heart failure, myocarditis, and pulmonary embolisms with thrombus are a few of the cardiovascular complications of COVID-19 where cardiac POCUS has proven useful during the pandemic [29]. However, no technology comes without pitfalls [21]. The operator-dependency on producing and interpreting accurate and precise images is a common problem frequently encountered in clinical practice [21,23]. This has made way for new technological and practical solutions to this dilemma.

Limitation of 2D Echocardiography

One of the principal indications for echocardiography in clinical practice is the assessment of the LV chamber size and the systolic function [30]. Typically, this assessment involves direct visualization and interpretation of the dynamic ultrasound to estimate the LVEF. If these interpretations were to be done using 2D echocardiography, certain assumptions regarding geometric remodeling of the left ventricle would be necessary [30-32]. One of the limitations of standard 2D echocardiography is referred to as the missing "third dimension". The difficulty of endocardial visualization is most challenging in the apical-lateral segments, which can be compensated for by certain maneuvers with the transducer (i.e., lifting). Furthermore, 3D technology allows for frame-by-frame detection of the endocardial surface from real-time 3D datasets. Numerous studies have shown that compared to 3D echocardiography, 2D echocardiography may underestimate left ventricular volumes [32]. In a study of patients with LV dysfunction due to previous myocardial infarction, patients underwent serial real-time 3D echocardiographic measurements and had low test-retest variability but, they were able to detect small changes in LV volumes that could not be detected by standard 2D echocardiography [33]. The Disparity in measurements between 2D and 3D echocardiography has been different between various studies, suggesting a probable error in the measurement methodology.

A large multi-center study focused on identifying potential errors in the measurements, found that the major source of underestimation of volume was the tracing method and the limited spatial resolution of real-time 3D echocardiographic imaging [33]. There was a correlation between RT3DE-derived LV volumes and CMR imaging (EDV: $r=91$, ESV: $R=0.93$), but were found to be 26% and 29% lower consistency across different institutions. The reason for this was found to be that RT3DE cannot differentiate between the myocardium and the trabeculae [33].

AI in Echocardiography and POCUS Interpretation

Although concrete recommendations are available for interpreting echocardiography and cardiac POCUS, these techniques are still prone to a considerable number of subjective errors [34,35]. Besides the fact that there can be interpersonal differences in the initial imaging interpretation, interpretation differences can also exist for the same person upon repeated readings [36]. This frequently encountered pitfall has prompted the use of different technologies to avoid misdiagnosis. AI has the potential to obtain images, process them

and accurately interpret them constantly and repeatedly. AI also has the ability to improve diagnostic accuracy, clinical management, and patient care accuracy [36]. Besides accuracy, AI also reduces human strain, especially for inexperienced echocardiographers. It typically takes a sonographer approximately 1-2 years to comprehend and accurately put into practice the basic concepts and techniques of echocardiography [36]. With AI, programmed standardization can reduce assessment time and improve beginner's accuracy. Additionally, this technology has the potential to improve operational efficiency in non-echocardiographic settings, such as emergency departments, and can also be used by resident physicians as a rescue measure in the appropriate clinical scenarios [37]. Furthermore, time restraints may prove challenging, particularly if the patient presents with an infectious pathology or due to the sheer volume of patients at a medical center.

This may cause a delay in the diagnosis and skew prompt medical management. According to a single-blinded, nonrandomized, cross-sectional investigation involving clinicians with varying POCUS expertise, non-cardiologists practicing cardiac POCUS can reliably detect common causes of heart failure [38]. POCUS is increasingly recognized as a paramount technique, especially in the training of resident physicians for monitoring cardiac function. POCUS has achieved some of the most significant advances in the management of critically unstable patients due to its capacity to evaluate pathology in real-time at the bedside [38]. POCUS is also frequently utilized to investigate unexplained hypotension, arrhythmia, or difficulties with equipment such as ventricular support devices or extracorporeal membrane oxygenation [38]. Despite its accomplishments, POCUS has operator restrictions, principally as it is often performed by non-cardiologists and non-expert physicians [37,38]. As patients decompensate and the window for accurate medical management closes, these restrictions become increasingly important. The integration of AI intends to address some of these pitfalls, allowing doctors to create faster evaluations with more input data and obtain accurate diagnostic and treatment recommendations ultimately aiming to improve patient outcomes [39].

Consequently, when discussing AI in cardiac ultrasound (US), several techniques have emerged to improve outcomes.

For example, the use of AI for global longitudinal strain (GLS) assessment has significantly enhanced results [40]. The AI software was able to accurately identify cardiac images, conduct precise timing of cardiac events without human input, assesses the myocardium, estimates motion and eventually quantifies GLS, irrespective of a wide range of left ventricular (LV) function and picture quality [40]. The most extensively used semi-automatic speckle-tracking algorithms require multiple phases of operator input, with a single GLS analysis is said to take between 5 and 10 minutes to complete. On the other hand, AI assessment takes less than 15 seconds [40]. Left ventricular (LV) function, including ejection fraction (EF) quantification, is accurately conducted [40]. Other assessments performed during

cardiac US have also been positively influenced by AI. AI-driven echocardiographic imaging analysis approaches done by automated contour-based segmentation have proven incredibly useful [41,42]. Asch et al. utilized a software called AutoEF and Baylabs to perform automated left ventricular ejection fraction (LVEF) calculations [43]. The approach demonstrated similar accuracy to measures taken by cardiologists with more than 20 years of expertise, as shown in a study of 99 patients [43]. Additionally, human experts trained the AI with a database of over 50,000 echocardiographic studies from the Minneapolis Heart Institute spanning a period of 10 years. Expert readers' visual EF corresponded highly with the AI response ($r=0.95$ ($P<0.001$; CI, 0.938-0.960), ICC =0.92 (CI, 0.90-0.936) [43].

This was comparable to the accuracy of three board-certified, expert readers: $r=0.94$ ($P<0.001$; CI, 0.925-0.952), ICC =0.90 (CI, 0.876-0.920) [43]. The AI completed the analysis in 1 to 5 seconds per patient with a high level of consistency [43]. Without extensive operator expertise, distinct physiological and pathological situations may exhibit similar characteristics that are challenging to differentiate. For instance, left ventricular hypertrophy is common among athletes, but it can also be detected in hypertrophic cardiomyopathy (HCM). Because hereditary cardiac illness has a higher risk of sudden cardiac death, a precise distinction is crucial [35]. After adjusting for age, Narula et al. developed an ensemble technique using support vector machines and artificial neural networks to accurately distinguish between these two conditions, achieving a sensitivity of 96% [44]. Additionally, the assessment of regional wall motion abnormalities (RWMA) for the treatment of ischemic coronary artery disease is a common examination in echocardiography [40]. Recently, a study examined a deep learning method to construct automated diagnostic models for myocardial infarction. The area under the receiver-operating characteristic curve (AUC) of a deep learning system for detecting the presence of RWMA was comparable to that of a cardiologist/sonographer interpretation and significantly higher than that of resident readers. Except for the left anterior descending coronary artery, deep learning demonstrated relatively low rates of misclassification of the right coronary artery, left circumflex coronary artery, and control groups [32].

Zhang et al., using PLAX- and A4c-view videos, trained a multi-layer technique to identify HCM using a cohort of patients with HCM (with varied patterns of LV thickness) and technically matched controls [45]. Instead of constructing a discriminative model based on hand-selected features, the technique establishes a black-box model wherein the training algorithm manages all the feature derivation and selection. With a C statistic (area under the receiver operating characteristic curve) of 0.93 (95% CI, 0.91-0.94), the model accurately detects HCM. Subsequently, they developed a model to identify cardiac amyloidosis, a disease with similar morphologic characteristics, but different in etiology. They trained an AI model to detect cardiac amyloidosis using amyloid patients and matched controls and obtained outstanding results, with a C statistic of 0.87 (95 percent CI, 0.83-0.91) [45]. Similar to HCM, they observed that subjects with a greater

projected risk of amyloid had larger LV mass ($\rho=0.36$, $P=0.002$) but did not exhibit increased left atrial volumes ($\rho=0.12$, $P=0.31$) [45]. These technologies have the potential to be applied in cardiac US for increased precision, removing the need for an expert operator in select cases. Additionally, by alleviating time constraints, physicians have increased safety precautions especially when dealing with unstable, combative, or highly infectious patients. Artificial intelligence algorithms can provide extreme value in capturing high-dimensional information that is not easily perceptible to the human eye, as well as maximizing the extraction of image features.

Through this process, AI can help to identify crucial cardiac anatomical structures, improve the accuracy of cardiac segmentation, and help with the assessment of cardiac functioning [46]. Therefore, the cardiac imaging assessment of COVID-19 patients should be performed promptly without compromising diagnostic accuracy. AI has the potential to expedite this process by providing more consistent analysis for echocardiographic images [47]. Additionally, according to a prospective study which compared the cardiorespiratory parameters and time duration for assessment between Vscan Extend and the conventional US machine, this modality proved incredibly useful during the pandemic [48]. Vscan Extend is a handheld ultrasound device with a dual probe and an AI application software to precisely detect EF. In COVID-19 patients, the Vscan Extend portable US instrument aided in the quick detection, evaluation, and diagnosis of cardiopulmonary complications due to COVID-19 [48]. The Vscan Extend handheld US device's agreement with the traditional approach demonstrated its efficacy and safety [48]. On a large scale, integrating this device into daily practice, both in COVID-19 patients and different clinical settings, could alleviate the load on the healthcare system by aiding in quick diagnosis and requiring fewer resources for an initial cardiopulmonary examination [47]. However, many questions remain unanswered due to the lack of randomized control trials. More clinical data in the upcoming years will elucidate additional potential applications for AI in cardiac ultrasonography and the validity of current utilization trends.

Ultrasonographic Assessment in COVID-19 Patients

POCUS can play a crucial role in the clinical setting by assisting in the diagnosis of common causes of poor oxygenation and hemodynamic instability in critically ill COVID-19 patients, including cardiac arrest [49]. Common findings that can be identified using POCUS in COVID-19 patients include confluent and inferior lung field lesions, thickened/irregular pleural lines, subpleural consolidations, and air bronchograms [50]. Huang et al. used lung ultrasound to evaluate pulmonary lesions in 20 patients who were not critical at the time in a hospital in China. They concluded that ultrasound may be superior to computed tomography in detecting small peri pulmonary lesions and effusions [51]. Lung ultrasound proves invaluable in practical setting for managing COVID-19 patients, allowing for the assessment of pulmonary complications/abnormalities, assess perioperative

pulmonary status evaluation and guide ventilation management. Ultrasound can also confirm adequate endotracheal tube positioning, assessing for proper central venous catheter (CVC) placement, and rule out pneumothorax after CVC insertion [52]. Lung ultrasound has demonstrated high overall diagnostic sensitivity and specificity in COVID pneumonia [53]. While COVID pneumonia predominantly affects the posterior-basal lung zones, POCUS/LUS provides an effective view of the lung's peripheries [54]. Particularly in Covid-19, B-Lines are most commonly visualized in the posterior-lateral lung zones in the early stages of the disease [55].

POCUS is particularly useful in evaluating cardiac involvement in COVID-19 cases. It is well-established that COVID-19 can damage the myocardium either by activating the immune cascade or via primary viral infection, affecting cardiac function by myocarditis or pulmonary embolisms [56]. The highest accuracy of POCUS in these settings is obtained when used to evaluate left and right ventricular function, valvular dysfunction, pericardial effusion and to calculate stroke volume [56].

Use of AI beyond the COVID-19 Era

In addition, AI in echocardiography and POCUS, can be used to calculate LV systolic function, and will continue to be of the most important uses of this technology. Knackstedt et al. tested a fully automatic software employing machine learning-enabled image analysis [57]. The autoLV can provide biplane end-diastolic and end-systolic volumes in a more feasible way in 98% of studies with an estimated time of 8 seconds/ patient. This means that automated analysis can provide quick and reliable EF measurements via LVEF and LV strain [57]. Cannesson et al. also explored the use of AI in calculating EF in 218 patients, demonstrating strong correlation with manual measurements ($r= 0.98\%$), with far less time (48.2 s vs 102.2; $p<0.01$). When compared to visual estimates by expert readers, it correlated well ($r= 0.96$; $p<0.01$) [58]. A newly released Venue platform that can calculate velocity time integral and cardiac output in real time. Real-time visualization of this data can be time saving and improve prompt adequate decision making by clinicians [59]. Bobbia et al. determined in an experimental study that the Venue Auto-VTI tool had a better correlation with cardiac output measurement by thermodilution than any manual measurement [59]. The new echocardiographic techniques allow for the accurate assessment of mechanical properties of the myocardium, especially strain or deformation. Moreover, myocardial strain has been shown to offer more accurate measurement of systolic function compared to manual cavity measurement parameters.

These methods have been used in various clinical scenarios including cardiomyopathies, oncologic cardiology and to detect the presence of cardiac remodeling. These techniques also allow clinicians to recognize various myocardial strain patterns that can correspond to different disease processes [60]. Furthermore, machine learning-augmented interpretation aids in distinguishing between

diseases with similar echocardiographic characteristics. Sengupta et al. used clinical and echocardiographic data of patients with constrictive pericarditis and restrictive cardiomyopathy to develop an associative memory classifier (AMC) based algorithm. This was possible with the addition of speckle tracking echocardiography, obtaining the diagnostic area under the curve of 89.2% [61]. Another potential advantage of employing AI in echocardiography is the assessment of valvular pathology. In a study by Moghadassi et al., mitral regurgitation severity was approached by utilizing binary patterns as image descriptors which include details from different viewpoints of the heart using KNN (k-nearest neighbors) clustering and SVM (support vector machine), with an accuracy of 99.52%, 99.38%, 99.31% respectively. These findings corresponded to a sensitivity and specificity of 99.38% and 99.63% [62]. Lastly, many of the common cardiovascular diseases have been called heterogenous, with many genetic, pathological and socioeconomic factors in effect [63].

There can be many ML algorithms that can be utilized to identify the numerous subtypes using databases in echocardiography. Sanchez-Martinez et al. conducted a study in 150 patients aged >60 years old to evaluate for measurement of LV function at rest and during stress echocardiography in order to assess for differences between heart failure with preserved ejection fraction and healthy patients. The data that was utilized was acquired from the MEDIA study (metabolic road to diastolic heart failure). The machine learning algorithm was used to categorize patients, with a clinical validation performed afterwards. The correlation gave encouraging results (72.6%; 95% confidence interval, 58.1-87.0) [64].

Conclusion

Artificial intelligence (AI) has become an essential tool in modern medicine, particularly in the field of echocardiography. The use of AI is paramount in contexts characterized by time constraints, limited resources or patients with infectious comorbidities where fast and accurate cardiovascular evaluations are imperative. Undoubtedly, AI algorithms improve the interpretation of echocardiograms and point-of-care cardiac ultrasounds (POCUS), offering timely diagnosis and optimization of the management of cardiovascular complications related to COVID-19. Although its utility is evident, further comprehensive research is needed to validate, generalize and refine its use in various clinical settings. Additionally, its application in the post-covid era is still an exciting prospect. Artificial intelligence is here to stay and revolutionize cardiovascular healthcare, improving diagnostic accuracy and improving patient outcomes, which is at the heart of our medical practice.

Conflict of Interests

We hereby attest that all authors included in this manuscript have no conflict of interests

Source of Supports

None to disclose.

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