



## Comprehensive Review

# Role of Artificial Intelligence in Congenital Heart Disease and Interventions

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## ABSTRACT

Artificial intelligence has promising impact on patients with congenital heart disease, a vulnerable population with life-long health care needs and, often, a substantially higher risk of death than the general population. This review explores the role artificial intelligence has had on cardiac imaging, electrophysiology, interventional procedures, and intensive care monitoring as it relates to children and adults with congenital heart disease. Machine learning and deep learning algorithms have enhanced not only imaging segmentation and processing but also diagnostic accuracy namely reducing interobserver variability. This has a meaningful impact in complex congenital heart disease improving anatomic diagnosis, assessment of cardiac function, and predicting long-term outcomes. Image processing has benefited procedural planning for interventional cardiology, allowing for a higher quality and density of information to be extracted from the same imaging modalities. In electrophysiology, deep learning models have enhanced the diagnostic potential of electrocardiograms, detecting subtle yet meaningful variation in signals that enable early diagnosis of cardiac dysfunction, risk stratification of mortality, and more accurate diagnosis and prediction of arrhythmias. In the congenital heart disease population, this has the potential for meaningful prolongation of life. Postoperative care in the cardiac intensive care unit is a data-rich environment that is often overwhelming. Detection of subtle data trends in this environment for early detection of morbidity is a ripe avenue for artificial intelligence algorithms to be used. Examples like early detection of catheter-induced thrombosis have already been published. Despite their great promise, artificial intelligence algorithms are still limited by hurdles such as data standardization, algorithm validation, drift, and explainability.

## Introduction

Artificial intelligence (AI) is a rapidly developing technology that has already affected many aspects of our lives, often in the background and unseen. Many lessons have been learned, and with improvements in computing power, the capabilities have grown exponentially in recent years. This is especially true in areas related to health care that directly affect diagnosis and management and have led to advanced predictive algorithms based on large data. But, how do we as medical professionals embrace this technology and help ensure its proper development and implementation?

AI in health care needs to become approachable for the medical community at large. These are the teams who must frame the questions to be solved and who are responsible for the practical delivery of care. At present, the majority of physicians limit their interaction with AI to chatbots that aid in a speedy

literature search or to rapidly compile a list differential diagnoses. But, the potential of AI offers so much more, especially in a field such as congenital heart disease (CHD), which is highly variable and complex and uses a number of diagnostic and therapeutic modalities.

To date, a limited use of AI in the diagnosis and treatment of CHD has been demonstrated, mostly focused on imaging algorithms for diagnosis and emerging possibilities in postoperative management. This is due to the fact that these are the largest data sets for analysis in this patient population. To truly harness the potential of AI, we must perform large-scale studies analyzing outcomes data to power the analysis of these relatively infrequent conditions. Until international collaboration occurs to provide the numbers to power studies, CHD will continue to be a field whose practice is based on institutional knowledge. Therefore, to initiate a conversation about AI in CHD, it is important to understand what information currently exists with a cursory search on the topic.

**Abbreviations:** AI, artificial intelligence; CCT, cardiac computed tomography; CHD, congenital heart disease; CMR, cardiac magnetic resonance; CNN, convolutional neural networks; CRT, catheter-related thrombosis; CVP, central venous pressure; DL, deep learning; ECG, electrocardiogram; ML, machine learning.

**Keywords:** artificial intelligence; congenital heart disease; deep learning; interventional cardiology; machine learning; structural heart disease.

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## Search: what are the uses of AI in CHD?

### ChatGPT output

AI has promising applications in the field of CHD, enhancing diagnosis, treatment, and patient management. The following are some key uses:

1. Early detection and diagnosis: AI algorithms can analyze medical imaging (such as echocardiograms, magnetic resonance imaging, or computed tomography [CT] scans) to identify structural heart defects more accurately and quickly than traditional methods.
2. Risk assessment: Machine learning (ML) models can evaluate patient data to predict the likelihood of complications, guiding personalized treatment plans and improving outcomes.
3. Treatment planning: AI can assist in creating individualized surgical plans for patients with complex heart conditions by simulating various surgical approaches and outcomes.
4. Monitoring and management: Wearable devices equipped with AI can monitor patients' heart rhythms and vital signs in real time, alerting health care providers to potential problems early.
5. Research and drug development: AI can analyze vast amounts of genomic and clinical data to identify new targets for drug development and understand the underlying genetic factors of CHD.
6. Telemedicine: AI-based platforms can facilitate remote monitoring and consultations, making it easier for patients in remote areas to receive care from specialists.
7. Patient education and support: AI-driven chatbots and informational tools can provide patients and families with tailored educational resources about CHD, improving their understanding of the condition and care options.

Our aim is to discuss some broad categories of current investigation, which hold great promise in the use of AI to improve diagnosis, management, and delivery of health care for patients with CHD.

## ML in noninvasive cardiac imaging

Cardiovascular imaging is integral to the diagnosis and follow-up of patients with CHD and acquired heart disease and is now being transformed by AI that can enhance diagnostic accuracy and offer insights into cardiovascular health through advanced computational techniques. Pediatric imaging is challenging because the structures are small, the heart rate is fast, and the questions are difficult. This makes it a perfect field for developing new AI-based solutions. Early AI software for imaging relied on rules-based algorithms, often referred to as symbolic or classical AI. However, the increase in AI adoption is based on ML, specifically, deep learning (DL). Unlike classical AI, ML algorithms learn patterns to make inferences directly from the imaging data without a pre-existing model. DL, inspired by the structure and function of the human nervous system, uses deep artificial neural networks to process complex data sets. DL applications are in use for echocardiography, cardiac magnetic resonance (CMR) imaging, and cardiac computed tomography (CCT). Many of these models are developed specific to a modality agnostic to the use case.

### Echocardiography

In echocardiography, the diagnostic information is embedded in planar cine image sets where views are not explicitly labeled. Although ultrasound offers superior temporal resolution compared to CCT or CMR, echocardiographic images suffer from its lower signal-to-noise

and contrast-to-noise ratios, geometric dependence, and significant quality variability due to differences in patient-specific acoustic windows. Consequently, significant effort has been applied to DL for identifying echocardiographic views or improving evaluate image quality.<sup>1-3</sup>

DL echocardiography research has focused on automating assessment of ventricular structure and function and identification of pathology. Zhang et al<sup>1</sup> developed a fully automated system using convolutional neural networks (CNNs) for cardiac structure segmentation, chamber planimetry, and classification of myocardium with specific application to hypertrophic cardiomyopathy and pulmonary arterial hypertension.<sup>1</sup> They were able to show the power of automated analysis, essentially eliminating interobserver variability from the interpretation. In a landmark study, Ouyang et al<sup>4</sup> reported a 3-dimensional (3D) CNN for beat-by-beat assessment of left ventricular ejection fraction, which outperforms all manual tracing with astounding speed. It is particularly effective in patients with arrhythmias.<sup>4</sup> This DL approach provides multibeam analysis in a fraction of the time required by a sonographer, while reducing both intraobserver and interobserver variability. For structural heart disease, DL models have been trained on echocardiogram clips for the automated diagnosis of atrial septal defects, ventricular septal defects, and coarctation of the aorta.<sup>5,6</sup> DL models have demonstrated sensitivity and specificity up to 76% and 88%, respectively, in diagnosing atrial septal defect compared with pediatric cardiologists who demonstrated sensitivity and specificity of 53% and 67%, respectively.<sup>7</sup> There have been few complex CHD-specific applications, but Diller et al<sup>8</sup> developed a CNN framework capable of distinguishing echocardiograms with a systemic right ventricle from those with a systemic left ventricle or normal anatomy. Although the study had 98% accuracy, the CNN algorithm has not been externally validated for clinical deployment—a very common scenario for the numerous algorithms being generated in the literature. Many of the developed algorithms are difficult to transfer to other institutions because they rely on bespoke image formats and preprocessing. As an example of another echocardiography application, Tromp et al<sup>9,10</sup> showed that ML can assess transvalvular gradients and characterize diastolic dysfunction with adequate accuracy and reliability.<sup>9,10</sup>

Machine learning has been applied to fetal echocardiography with the goal of increasing accuracy and access in low resource settings.<sup>11-13</sup> ML has proven accurate and efficient for fetal heart screening in regions with limited access to cardiologists.<sup>14</sup> For example, fetal intelligent navigation echocardiography is a novel fetal echocardiography technology that obtains 9 standard views and, based on the acquired images, provides a statistical likelihood interpretation. The technique has modest predictive value but is a useful screening paradigm.<sup>15,16</sup> Unfortunately, few studies extend DL methodologies to complex CHD, transesophageal echocardiography, or 3D echocardiography—all areas for further development. Looking forward, developing CHD-specific AI algorithms could reduce image acquisition times, enhance image processing, and improve diagnostic accuracy, with the eventual goal of near operator-independent acquisition and AI-assisted diagnosis. Algorithms using self-supervised and semisupervised learning approaches, which function effectively with limited labeled data, hold particular promise for CHD applications.

### CMR and CCT

and CCT lend themselves to ML because they rely on complex acquisition strategies, including multidimensional contrast

mechanisms, as well as the need for accurate and reliable segmentation and quantification of biomarkers based on acquired data, to help guide diagnosis and therapy management. The optimal DL models for both yield superior results by leveraging the full 3D structure of the data. The dynamic range and complicated noise characteristics of CMR and CCT data require specialized preprocessing routines. The most well-developed group of ML applications is image segmentation—the process of assigning labels to regions of the image based on their anatomic structure. This includes image processing for CMR planimetry and making 3D models from CCT data sets. Several groups have successfully developed DL-based segmentation algorithms tailored for CHD cases.<sup>17</sup>

DL analysis has been most extensively applied to CMR, specifically for cardiac chamber segmentation to assess structural and functional parameters. This is partly due to the availability of high-quality public CMR data sets and online data science competitions. One remarkable effort involved training a fully convolutional neural network (FCNN) using data from nearly 5000 CMR scans from the UK Biobank, with remarkable segmentation accuracy with a mean absolute error of <10 mL (1%-5%) for all chambers.<sup>18</sup> Again, there have been few congenital specific applications, but Tandon et al<sup>19</sup> demonstrated that a CNN initially trained for endocardial and epicardial segmentation of structurally normal hearts could be adapted for use in repaired tetralogy of Fallot, with a relatively small new training data set.<sup>19</sup> They proposed that a similar approach could be extended to other forms of CHD, allowing broader application of DL in pediatric and adult congenital cardiology. Other CMR DL applications have targeted specific pulse sequences and analyses. For example, Fahmy et al<sup>20</sup> used an FCNN for automated myocardial T1 sequence segmentation and mapping, and Zhang et al<sup>21</sup> developed a system for myocardial scar delineation using noncontrast cine acquisitions and T1 maps. This myocardial characterization without gadolinium contrast administration showcases the promise of ML to create synthetic contrast-enhanced CMR resulting in safer more efficient CMR studies. This is of particular importance in pediatrics where brain gadolinium deposition is a concern.

Research on DL applications for CCT has predominantly focused on segmentation and analysis of coronary CT angiography. Coenen et al<sup>22</sup> demonstrated that a DL-based algorithm for noninvasive fractional flow reserve (FFR) estimation using coronary CT angiography significantly improved the accuracy of identifying functionally obstructive coronary artery disease compared with visual assessment (78% vs 58% accuracy per vessel).<sup>22</sup> There are now hundreds of publications describing new segmentation techniques—few are specifically applicable to CHD. Li et al<sup>23</sup> described a unique algorithm for segmenting the entire human aorta using a 3D nnU-net DL method. They were able to overcome noise in nonideal images and inhomogeneous opacification in generating highly representative segmentations without supervision.<sup>23</sup> In attempting to extend the ML to outcome prediction from CT images, Eisenberg et al<sup>24</sup> employed a previously established FCNN for intrapericardial segmentation on CCT to quantify epicardial adipose tissue volume, which enhanced the predictive value of coronary calcium scoring for major adverse cardiovascular events.

Probably, the most innovative applications that are not segmentation include the use of DL for image reconstruction from raw data for both CMR and CCT. With advances in ultrafast image reconstruction have come both artifact reduction and denoising. For instance, Wolterink et al<sup>25</sup> used a generative adversarial network to denoise low-dose CT images, achieving results comparable with those of full-dose CT scans. This is of particular interest in pediatric heart disease given the concern about age-dependent susceptibility

to ionizing radiation.<sup>25</sup> Similarly, Fan et al<sup>26</sup> developed an FCNN for reconstructing undersampled CMR data, reducing reconstruction time by up to 14-fold compared with that of traditional already accelerated methods. Rapid CMR imaging allows for either more nonsedated cases or substantively shortening the time of anesthesia required. These applications underscore a critical advantage of DL: training the model is computationally intensive, but once trained, it can perform inference faster than conventional rules-based algorithms, possibly yielding significant efficiencies in clinical workflows. Both of these are examples of applications initially developed for adult imaging that could have a profound effect in pediatric cardiology.

ML, and DL in particular, is beginning to be applied to different types of cardiac imaging. Besides image interpretation, there are many tasks in the imaging process that can potentially benefit from application of ML. In the short term, ML techniques are highly likely to be incorporated in the image acquisition and reconstruction domains, in the postprocessing workflow and analysis of advanced image features beyond visually identifiable features as well as multidimensional contrasts and their interpretation. One promising method is to use DL methods to simulate images, both to augment the size and the variability in the training data sets for segmentation and classification networks and to characterize bias between different imaging modalities. A CMR scar simulation method has recently shown to improve identification of scar in late gadolinium enhancement images. Another promising technique is reinforcement learning, in which an agent is trained by trial and error using feedback from previous actions and experiences.

Despite the aforementioned significant advances, there are currently no published clinical trials in which ML has been compared with human evaluation of CMR or CT data sets. Prospective controlled trials are required to establish the effectiveness of AI algorithms in clinical practice. Validation must be performed using data from the same cohort as was used in the training, but importantly from other cohorts. Algorithms must be validated with data from different centers and different acquisition devices. As the field moves forward, it is critical that the reference data be meticulously validated, in particular if the reference data are from clinical reports. The validation metrics are variable and case dependent but should include sensitivity, specificity, positive predictive value, and model parameters like area under the receiver operating characteristic (ROC) curve. To ensure the continued advance of AI in pediatric and congenital cardiac imaging, published algorithms should be available on open-source platforms enabling replication and benchmarking.

## Electrocardiograms as a cornerstone of clinical diagnostics

Today, the 12-lead electrocardiogram (ECG) is an essential and indispensable screening and diagnostic tool in cardiology. Its accessibility and ease of acquisition added to its diverse diagnostic capability guarantees its use in various clinical settings. Today, our uses for ECGs include the following:

- Diagnosis of arrhythmias
- Detection of myocardial ischemia and infarction
- Assessment of drug effects on cardiac conduction
- Assessment of cardiac anatomy and CHD
- Assessment of electrolyte abnormalities
- Diagnosis of hypertrophic and dilated cardiomyopathy
- Diagnosis of inherited arrhythmias and cardiac channelopathies

Although an effective tool, ECGs have many limitations. Namely, small acquisition variability can affect signal-to-noise ratio, alter vector

interpretation, or, in some cases, affect voltages acquired. Subsequently, analysis dependent on subtle variability among ECGs is extremely difficult. In addition, ECG analysis has been limited to perceivable changes in the electrogram.

Its use as a prognostic tool is similarly difficult. Attempts to predict mortality, hemodynamic events, and structural conditions as a screening tool across the population have not been reproducible or financially feasible. For this reason, it is currently not recommended as a broad screening tool to assess risk of sudden cardiac death in the general population where the pretest probability is low. In specific populations, however, it has proven useful. An example is adult patients with tetralogy of Fallot, where there are statistically and clinically significant differences of easily measurable variables such as QRS fractionation and duration.<sup>27</sup> With the advent of AI, suddenly, our ability to analyze subtle imperceivable changes has substantially increased.

## AI and ECGs

AI has proven useful in overcoming some of the inherent limitations of population wide electrocardiographic analysis. It provides an automated, time-efficient, and accurate tool to analyze subtle and imperceivable variabilities in the ECG. This has the potential to expand its use as a screening and prognostic tool.

Most algorithms currently in use for analysis of electrocardiographic signals are supervised DL models. Electrocardiographic data are processed akin to the analysis of pixels in image processing. Each millisecond on the ECG represents a voltage amplitude, a weight, when combined with its neighbors across the 10 seconds throughout the ECG, builds a time series matrix where each lead is represented as a long vector. This serves as the input layer of the neural network, a layer composed of multiple nodes.<sup>28</sup>

These nodes are then subsequently linked in multiple hidden layers where mathematical associations and derivations can be formed. Each connection is represented by various weights and biases that are adjusted during the training process to accurately classify the outcome of choice, the output layer, and to minimize the error between the predicted and true outcomes. In linear algebra, matrices and vectors create an opportunity for fast computational derivation using a parallel processor, in most cases a graphical processing unit, saving time and energy on large amounts of computation. This allows the model to separate data using multiple derivations and associations very quickly. Using large data sets, this naturally overcomes noise and subtle acquisition variations mentioned and increases our power to detect meaningful changes in the ECG in association with various conditions.

Because of its ability to make multiple levels of derivation and association, a model will always find a mathematical separation for the variable of interest no matter how complex. This is a double-edged sword as an overly complicated separation is likely not generalizable or clinically useful. This is why it is crucial to test and validate the model on data it was not exposed to, a testing data set, which usually comprises 20% of the research data set.

## The promise and impact of AI

With the promise of this expanded analysis of ECGs, we have had an array of articles demonstrating its application to augment our clinical screening and diagnosis.

### Use in arrhythmia diagnosis

One of the earliest uses of AI in ECGs was in detection of atrial fibrillation. Since atrial fibrillation was frequently asymptomatic but associated with significant risk of stroke, it was a diagnostic gap worth exploring. In 2019, Attia et al<sup>29</sup> developed a CNN able to analyze sinus rhythm ECGs and determine whether patients had ever had atrial fibrillation. They used a data set of 649,931 ECGs in 180,922 patients and separated the data set in the usual 80:20 for training and testing. Findings showed an area under the ROC curve of 0.87, with a sensitivity and specificity of 79%.<sup>29</sup> Moreover, the model performed better than the physician comparison group.

Then came the first prognostic use of ECGs through AI. Raghunath et al<sup>30</sup> showed that one could predict risk of atrial fibrillation in 1 year from a single ECG in patients who had never had atrial fibrillation. They similarly trained a CNN using 1.6 million ECG traces in 430,000 patients. Area under the ROC curve was similarly 0.85.<sup>30</sup>

### Use in diagnosis of left ventricular dysfunction

Perhaps, the most well-known and successful use of AI in medicine is its use to predict left ventricular dysfunction. More than the late changes associated with cardiomyopathy such as low voltage, AI has proven useful in categorizing and delineating dysfunction when using electrocardiographic signals. In 2024, Mayourian et al<sup>31</sup> produced a CNN model trained on an ECG–echocardiogram pair in pediatrics, which could accurately detect left ventricular dysfunction with an area under the ROC curve of 0.88. They used 92,000 ECG–echocardiogram pairs, and results were verified by external validation. They later verified these results specifically for the CHD population using 8584 ECG–magnetic resonance imaging pairs with an area under the ROC curve of 0.87.<sup>32</sup> This may prove valuable in long-term follow-up of pediatric cardiology patients, especially as a low-cost screening tool for risk stratification and supporting closer follow-up, imaging studies, or invasive hemodynamic assessment.

The article also specifically addressed the explainability of the model using saliency maps. The frequency by which the nodes in the hidden layers were used during testing was mapped back to the input layer and represented as a heat map on the 12-lead ECG. Although this does not provide the exact mathematical manipulation or derivation used, it does shed light on which parts of the ECG were most often used by the model and provides a small window of understanding.

### Use in mortality prediction

With the power for large-scale data processing, using ECGs to assess risk of mortality became achievable. In 2024, Mayourian et al<sup>33</sup> published a study in the *European Heart Journal* showing accurate 5-year mortality prediction in pediatric and adult patients with CHD using the 12-lead ECG. Interestingly, for more detailed subgroup analysis, they used a 50:50 split for training and testing data sets. Overall, 112,804 ECGs were used with an area under the ROC curve of 0.79. The model performed similarly on the temporal validation group. The extensive subgroup analysis shed some light on the limitations of the model and identified which congenital heart conditions the model was less effective at categorizing. The conditions with the lowest performance were complete atrioventricular canal defect and L-looped transposition of the great arteries. They hypothesized this is partly due to the abnormal baseline ECG associated with these conditions.

## Detection of CHD

Atrial septal defects have long been loosely associated with ECG findings such as incomplete right bundle branch block. Using a DL model, Mayourian et al.<sup>33</sup> demonstrated they can accurately classify the presence of an atrial septal defect using a 12-lead ECG. They used 92,377 ECG–echocardiogram pairs in the training data set and 12,631 in the testing data set. The area under the ROC curve was 0.84. This demonstrates a possibility for further classification of CHD using 12-lead ECGs.

With the advent of CHD newborn screening, the overall public health impact of an ECG-based screening tool for CHD is questionable. It can prove a good supplemental tool for screening in the newborn nursery. To date, there are no models to date that allow for screening of all CHDs based on 12-lead ECGs.

## Physiologic age

Interestingly, ECGs have been proven to accurately detect a patient's age and sex. Attia et al.<sup>34</sup> trained a model using a data set of 499,727 ECGs, which showed an area under the ROC curve of 0.97 and 90.4% classification accuracy. Moreover, various studies are showing a difference in chronologic age and predicted age, so-called cardiac age, in patients with various disease states.<sup>35</sup> This is indicative of their advanced physiologic age due to dysfunction and disarray and may represent a useful screening tool for the general population. Further research needs to be directed to provide a tangible understanding of the significance and association of long-term trend differences between the 2 age classifications.

## Challenges of AI use in electrophysiology

Model explainability reigns at the forefront of limitations when discussing any application of AI in medicine. Although limited methodologies have been developed, such as saliency maps, they still do not provide a full picture of what the algorithm is considering to categorize the population of interest.<sup>36</sup> Moreover, data quality, standardization, and preprocessing has been a rate-limiting step for generating new models. Finally, although many algorithms have been proven statistically significant, applying them to clinical workflow with long-term assessment of model sustainability and drift has been limited.

## Interventional procedures

Many of the reported uses for AI in interventional cardiology center around use of advanced imaging algorithms for image-guided navigation, automated 3D reconstruction, and prediction modeling for stent or device placement. However, the use of AI specific to interventions for CHD remains quite limited. One exciting example in general cardiology is the use of FFR derived from coronary CT angiography data sets to provide both anatomic and hemodynamic information to predict need for coronary intervention.<sup>37</sup> Previously, both an invasive cardiac catheterization with FFR obtained manually as well as CT angiography were required to obtain this same information. FFR derived from coronary CT angiography can be further used to provide enhanced procedural planning for percutaneous coronary intervention, which results in improved efficiency, reduced unnecessary testing, and lowered health care cost.<sup>28</sup> Similar benefits would seem to be achievable in structural interventions for large vessel disease, valve replacement, and septal defect closures in terms of planning and predictive

models based on enhanced analytics of both static and dynamic data.

Additional application of ML and DL on these large data sets could yield advances in robotic interventions and telemedicine-assisted remote interventions.<sup>28,38</sup> Digital method of image analysis allow for greater detail and visualization of target lesions, including the use of dynamic overlay to visualize dynamic structures in motion such as coronary arteries, cardiac valves, and others. The advancement in technology for virtual reality, touchless display, advanced robotics, and fast communication speeds with minimal latency allow for the real possibility of more routine attempts at remote surgery.<sup>38</sup> This sort of increased efficiency for a scarce resource would allow for the highest level of care even in areas typically underserved once properly equipped.

There remain many potential applications in CHD where rare lesions can be studied to devise treatment plans and optimize outcomes based on large data. These clinical decision-support systems could allow for accurate preparation and augmented care before any intervention and would presumably be superior to plans developed based on a single group's combined experience. Real-time monitoring to predict complications and early detection of complications has also been a focus of several projects.<sup>39,40</sup> Prediction of significant procedural complications would allow for proper risk stratification, allow for safety measures and additional resources to be available at the time of the procedure, and even determine the nature of the intervention should the risk analysis prove to be unfavorable. Validation of these algorithms is imperative but quite promising in the context of real-time monitoring and predictive analytics.

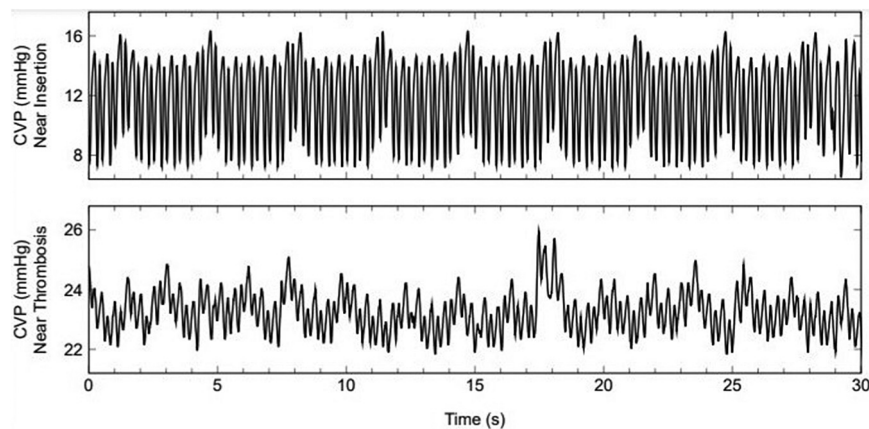
## Postprocedural monitoring and care

The application of AI technology to the cardiac intensive care unit (ICU) setting is most likely to manifest in the development of predictive algorithms derived from monitoring system data. The recording and storing of physiologic information is becoming much more common,<sup>41</sup> and this makes possible the retrospective analysis of all captured waveform information, and in some cases ventilator and pharmacy information as well. Without the recording of physiologic monitors, only that information visualized by bedside providers in real time is used, resulting in tremendous loss of valuable substrate for insight. Once high-frequency data are acquired, partnership between data scientists and caregivers can proceed toward identification of clinical problems or outcomes that would benefit from early detection.

After an outcome of interest has been selected for study, our approach is to examine the relevant physiologic waveforms for differences between the normative preoutcome period and the post-outcome period. Any observable differences are characterized by a set of features that permit discrimination between these periods. Next, we retrospectively query the entirety of the saved monitor data from the intervening interval. Artifactual changes are discarded using systematic criteria to facilitate accurate analysis. Supervised learning is then used to discriminate between the normative epoch and the epoch near the outcome. We can then ask clinically relevant questions such as “When did the identified waveform differences that triggered a probability alarm first become evident?”, “Is there sufficient warning time to engage in pre-emptive interventions, and what might those be?”, and “Are the alarms true early detections or are they false positives?”

An example of a clinical issue we addressed in this manner is that of central venous catheter-associated thrombosis. This is a common complication in the pediatric cardiac intensive care unit (PCICU) that can lead to loss of vascular access, pulmonary embolism, and cerebrovascular events. Patients in the PCICU are in a hypercoagulable state following





**Figure 1.**

**Observed difference in central venous waveform from time near catheter insertion to time of clinically detected thrombosis.** CVP, central venous pressure.

surgery, and the endothelial damage and stasis of blood flow that accompany the insertion of central venous catheters complete Virchow triad for thrombosis formation.<sup>42</sup> Indeed, pediatric patients undergoing surgery for congenital heart anomalies show a venous thromboembolism incidence of 2% to 18%.<sup>43,44</sup> Clinically, suspicion of thrombosis is aroused by clinical observations of edema, pain, tenderness, and phlebitis, and thrombosis is subsequently confirmed with ultrasound. However, almost 40% of thrombotic events are asymptomatic,<sup>45</sup> and frequent ultrasound surveillance is extremely costly. Once detected, thrombosis can be treated with thrombolytic or anticoagulation therapy or removal of the offending catheter. Thus, while detection of an established thrombus and treatment are relatively straightforward, initial suspicion relies solely on clinical recognition. This thwarts the opportunity for catheter-related thrombosis (CRT) prevention.

Our interest in catheter-associated thrombosis, beyond the required clinical management, was sparked by an initial observation of the central venous pressure (CVP) tracing. We noted that the gross appearance of the waveform was markedly different at the time of clinical thrombosis detection (swollen, plethoric extremity, and clot confirmed on ultrasound) compared with the tracing we typically see early after admission to the ICU shortly after line placement. This difference is illustrated in Figure 1.

We next identified children in our institution who had a history of CRT and central venous waveforms recorded in our high-frequency (125-Hz sampling rate) data capture system (Sickbay; Medical Informatics). Tracings were then deidentified for retrospective analysis. Since CVP signals are periodic, features based on the frequency representation of the signal were used to characterize it. However, CVP tracings contain artifacts from both impulsive noise (patient movement) and baseline drift (medication administration). Therefore, processing of the CVP data was required. Outliers were removed using robust estimates of means and SDs. After outlier removal, CVP waveforms from the period immediately after central venous line placement (when presumably there is no significant catheter-associated clot burden) and the period immediately before clinical confirmation of thrombus presence were used to train classification algorithms (eg, discriminant analysis) using a leave-1-out cross validation scheme. The trained classifier was then applied to the entirety of the signal that was left out (Figure 2A). The continuous classification score, resulting from the probability of the epoch resembling a thrombosis vs nonthrombosis period, was subsequently thresholded to generate a binary alarm (Figure 2B). In practice, this alarm could take the form of a traditional audible notification or a change in the clinical monitoring display.

We initially studied 20 patients in the Dell Children's cardiac ICU. The median age was 33 days at time of clinical CRT suspicion.

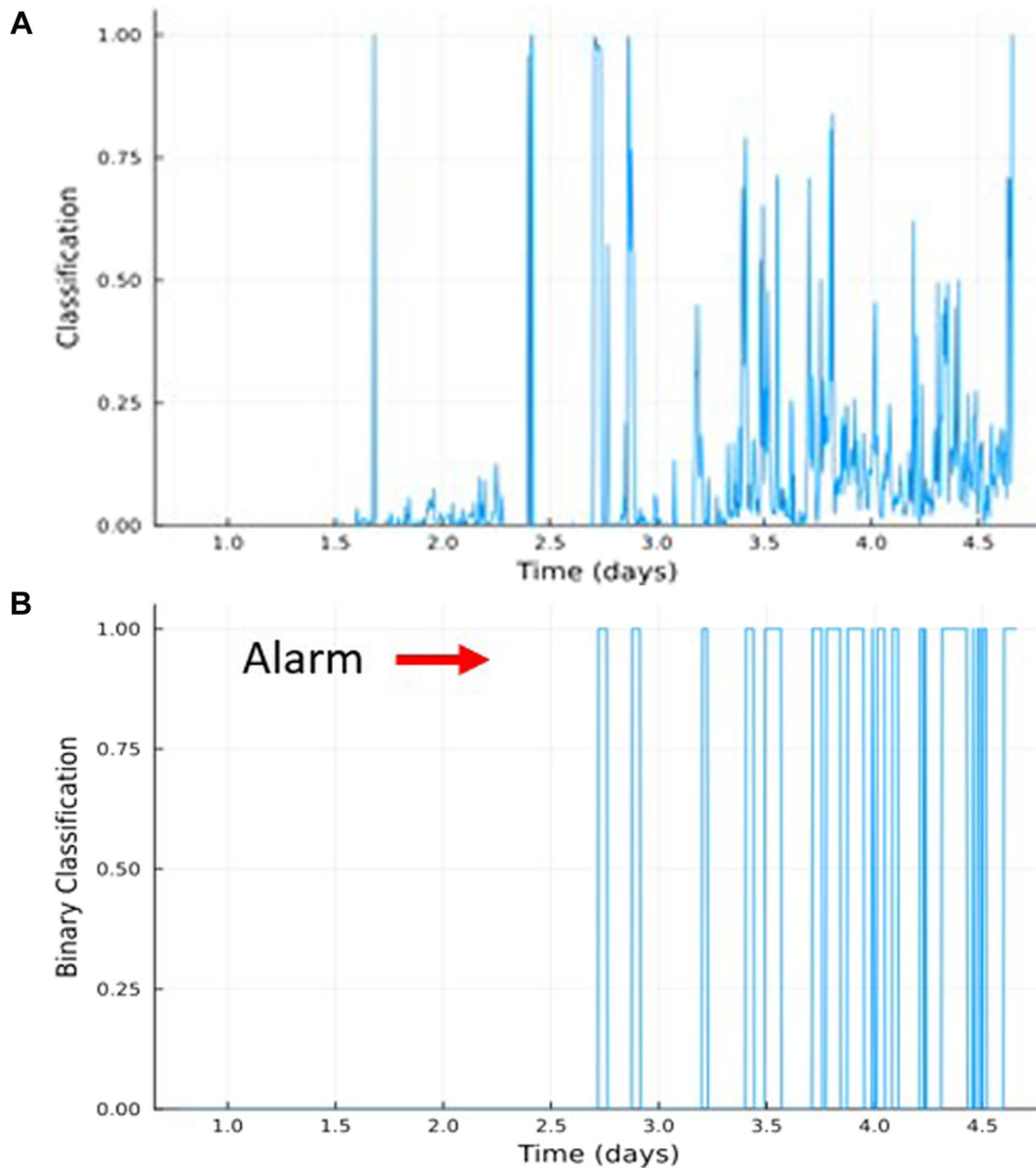
Ultrasound confirmed presence of central venous CRT in all cases. Children with CRT for >60 days after or <1 day after central line placement were excluded.

Manual curation of artifacts labeled approximately  $6\% \pm 3.5\%$  of data as noise in the 4 hours following catheter insertion. Based upon our set criteria, 90% of alarms were issued within 24 hours of CRT clinical symptomatology. While these results are promising, we are continuing to learn from false-positive alarms that permit hyperparameterization and algorithm refinement. Algorithm accuracy will also be enhanced in future efforts through incorporation of additional retrospective data from patients with CRT, and prospective, real-time clinical information from artifactual events such as patient movement and medication administration, and provider feedback on pragmatic rules for alarm silencing based upon diagnostic data. With this level of preliminary performance on patients with structural heart defects (and therefore atypical baseline CVP waveforms), similar techniques may be translated to general adult patients in the future using transfer learning techniques.

Another opportunity for use of physiologic data in the ICU comes from application of statistical process monitoring techniques, originally developed to assess batch industrial operations, to vital sign and hemodynamic information. We recently created multivariate control charts using statistical process monitoring for patients undergoing the arterial switch operation for d-transposition of the great vessels to establish adherence to a desired recovery pathway at each point as data were collected.<sup>46</sup> Trajectory maps were made by normalizing dynamic data, and then, statistical adherence to expected recovery was examined using multivariate monitoring charts coupled with leave-1-out crossvalidation (Figure 3).<sup>46</sup>

This approach shows promise for providing ICU clinical teams with advanced warning of patient deterioration based on previous recovery courses although it assumes that all patients recover in the same way from a particular surgery. Some subgroups may demonstrate deviations that are associated with faster recovery or different, but acceptable, progression. ML could be applied to further differentiate between positive and negative outcome pathways.

The field of critical care is increasingly moving toward development of predictive analytic models that use AI to provide decision support for early, pre-emptive intervention based on continuous patient monitor surveillance. Such physiologic surveillance cannot be easily accomplished by caregivers who are often subject to human limitations (eg, divided responsibility, distraction, and fatigue). Our approach to algorithm development in the PCICU relies on robust data capture systems, astute clinician observers, and close collaboration with data science/engineering colleagues.

**Figure 2.**

(A) The continuous classification score and (B) alarms generated from thresholding the continuous score.

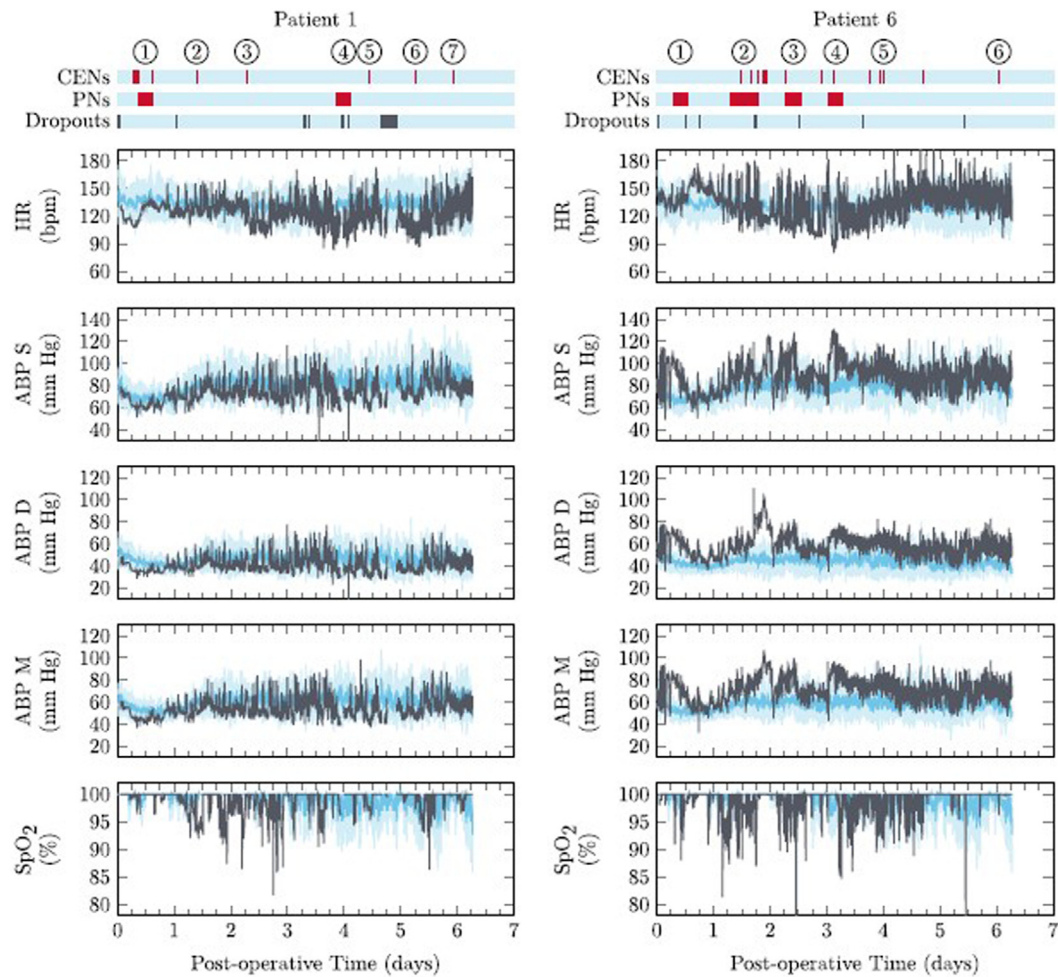
## Conclusion

Investigation into the use of AI and machine learning in pediatric cardiology or CHD is growing steadily, but pales in comparison to investigation in general adult cardiology (Central Illustration). Moreover, those efforts related to CHD are largely focused in the areas of cardiac imaging and monitoring, but limited translation to cardiac procedures and interventions. Inherent limitations for the use of AI in CHD remain the relatively small volume of patients and high rate of variability among those affected. Significant potential has been demonstrated in the areas of diagnosis via cardiac imaging, acute care management via monitoring algorithms, and predictive analytics for postoperative care via preoperative and postoperative patient characteristics. However, these advances were derived from the larger general cardiac population and mostly are not specific to the CHD population. In order to harness the power of AI, we need to maximize the volume of data specific to CHD, which is achieved only through global collaborations. This would allow AI to analyze large

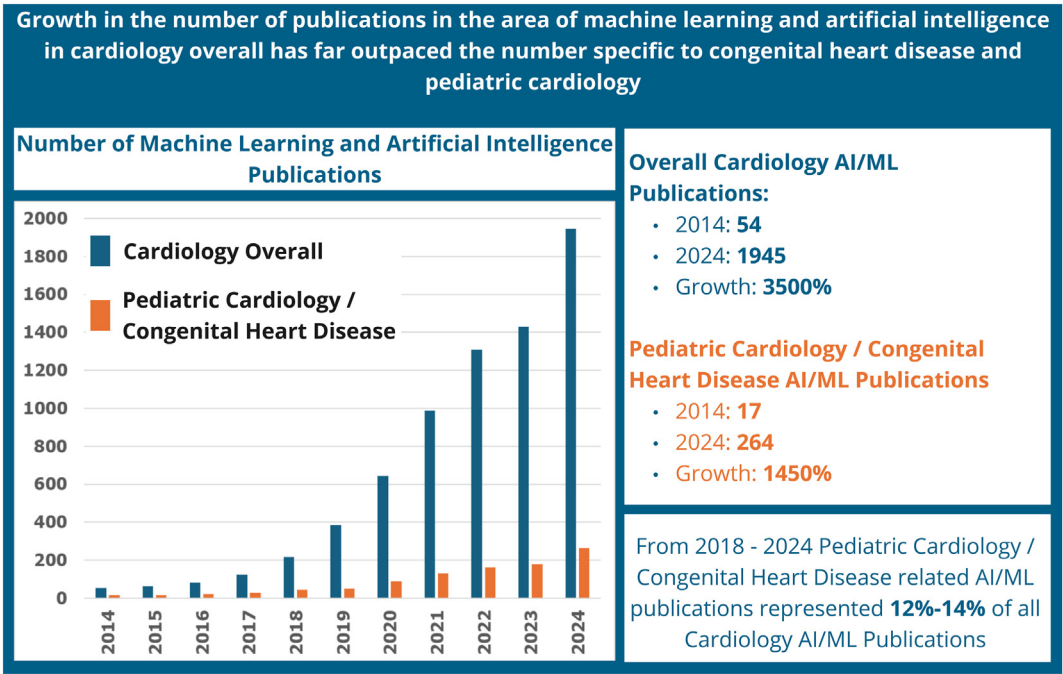
amounts of data with utilization of ML, DL, and neural networks and to use that information to improve health and care for patients with CHD. But, we must continue to strive for accurate and contemporary data, as the output for AI algorithms is dependent on the quality of the data input for analysis. These high-quality data sets from across the globe would minimize inherent bias related to numerous factors such as race, ethnicity, sex, and access to resources, to name just a few. There is incredible potential with this technology to deliver precise, tailored, and efficient health care in a way never imagined. It is up to our medical community to embrace this technology and ensure that it is not only accurate and reproducible but also accessible to all with CHD. Only then will the potential for AI be truly realized.

## Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, or publication of this article.



**Figure 3.** Postoperative monitoring for 2 patients. In each panel, the darker blue line indicates the mean trajectory of the patients other than the current patient and the lighter blue-shaded region indicates the region within 1 SD of this group. The dark gray lines indicate the measurements for the current patient. Spark charts for the clinical notes and dropouts are also provided. Patient 1 adheres to the trajectory well, whereas patient 6 deviates more significantly from the expected trajectory. ABP, arterial blood pressure; CEN, clinical event note; HR, heart rate; PN, progress note; SpO<sub>2</sub>, pulse oximetry. Reproduced from Howsmon et al.<sup>46</sup>



**Central Illustration.** Volume of publications on the topic of AI and machine learning in General/Adult Cardiology far outweighs those specific to Pediatric Cardiology or CHD. Discrepant growth continues to widen that gap each year.



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## Ethics statement

The authors retrieved and synthesized data from previously published studies; therefore, no ethical approval was required or obtained.

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