Title: Unlocking the potential of Artificial Intelligence in Sports Cardiology: does it have a role in evaluating athlete's heart?

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Abstract

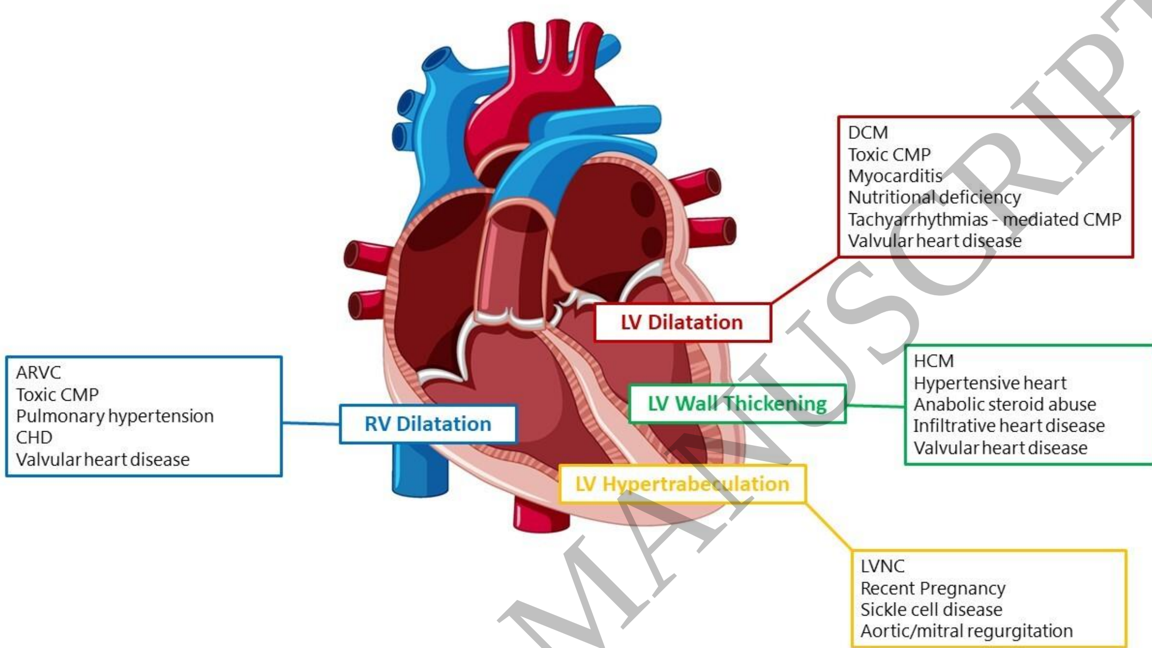
The integration of artificial intelligence (AI) technologies is evolving in different fields of cardiology and in particular in sports cardiology. AI offers significant opportunities to enhance risk assessment, diagnosis, treatment planning, and monitoring of athletes. This article explores the application of AI in various aspects of sports cardiology, including imaging techniques, genetic testing and wearable devices. The use of machine learning and deep neural networks enables improved analysis and interpretation of complex data sets. However, ethical and legal dilemmas must be addressed, including informed consent, algorithmic fairness, data privacy, and intellectual property issues. The integration of AI technologies should complement the expertise of physicians, allowing for a balanced approach that optimizes patient care and outcomes. Ongoing research and collaborations are vital to harness the full potential of AI in sports cardiology and advance our management of cardiovascular health in athletes.

Keywords: Artificial Intelligence; Machine Learning; Deep Learning; Sports Cardiology; Athlete's Heart; Cardiovascular Prevention

Introduction:

Sports cardiology is an emerging field that focuses on athletes' cardiovascular (CV) health. Although several efforts have been made to reduce the rate of cardiovascular events in athletes, sudden cardiac death (SCD) remains a relevant problem [1]. Physical activity (PA), if carried out regularly and for long periods, can result in substantial adaptations of the CV system. The athlete's heart results from these morphological, functional and regulatory adaptations and is characterized by increased wall thickness and cardiac dimensions in the presence of a normal systo-diastolic function [2] [3]. However, when physiological adaptations of the athlete's heart may overlap with certain pathological conditions there is the so-called "grey zone" (Figure 1) [4]. Therefore, accurately distinguishing between physiological and pathological cardiac adaptations in athletes can be challenging but crucial, as misdiagnosis can have significant consequences such as exclusion from competitive sports, false reassurance despite being at risk for SCD, and missed opportunities for effective therapeutic interventions [3]. Artificial intelligence (AI), even if nowadays little utilized and studied in this field, holds great potential in the field of sports cardiology by offering new tools for the early detection and prevention of CV disease in athletes while also assisting physicians in differentiating between physiological and pathological CV PA-related adaptations [5]. This article aims to explore the potential application of AI in the diagnostic approach to the athlete's heart, analyzing current literature and suggesting some areas of potential application.

Figure 1. Differential diagnosis in the grey zones of athletes' hearts between physiological and pathological cardiac adaptations to physical activity [4]

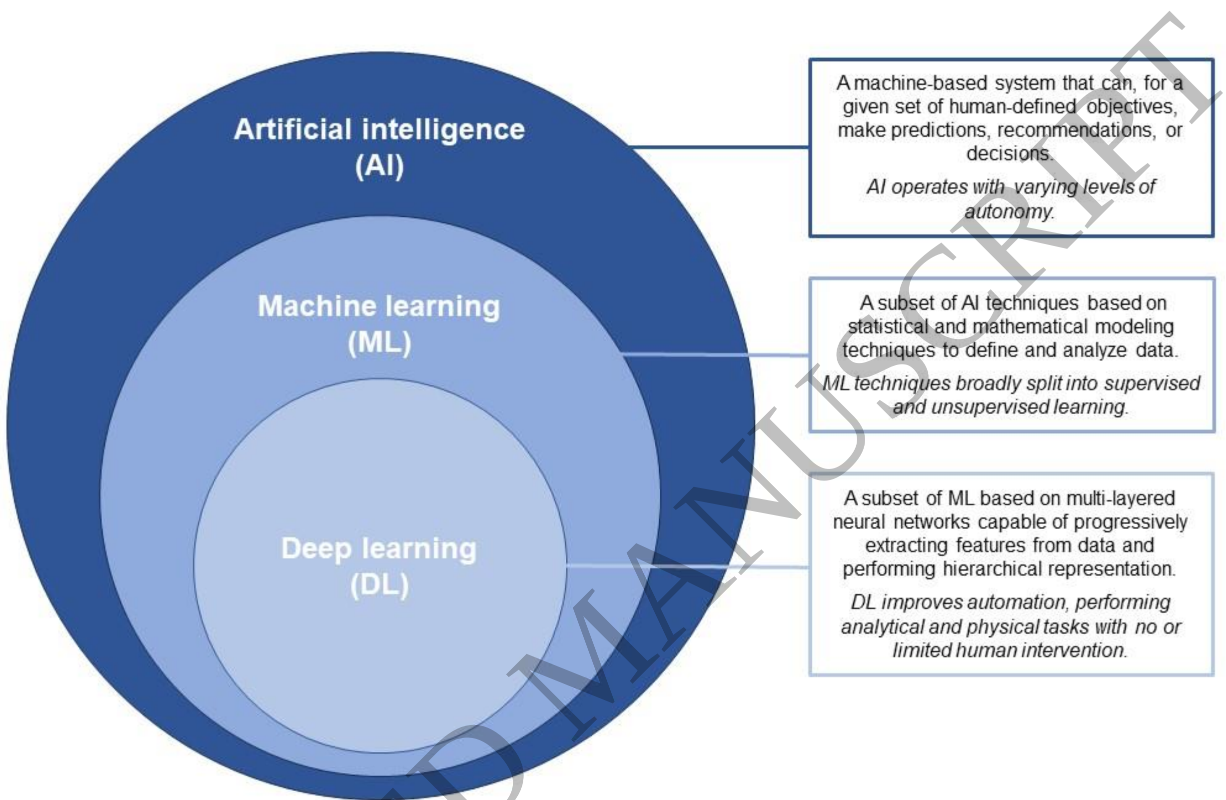


ACM: arrhythmogenic cardiomyopathy; CMP: cardiomyopathy; CHD: congenital heart disease; DCM: dilated cardiomyopathy; HCM: hypertrophic cardiomyopathy; LVNC: left ventricular non compaction

Artificial Intelligence, Machine Learning and Deep Learning

Although the birth of AI dates back to the 1950s, this field has gained tremendous momentum only in the last decade due to advancements in technology that have led to the widespread adoption of machine learning (ML) and deep learning (DL) methods. These methods have demonstrated a profound capability to sift through extensive medical data, discern patterns, make predictions, and assist in pivotal decision-making processes [6]. Even if the terms AI, ML, and DL are often used interchangeably, these are essentially hierarchically related [7] (Figure 2).

Figure 2. The hierarchical relationship between artificial intelligence, machine learning and deep learning



AI: artificial intelligence; ML: machine learning; DL: deep learning

AI refers to the performance of computer programs on tasks that are commonly associated with intelligent beings [8]. AI is built on algorithms and their coded instructions in machine-based systems in machines that can, for a given set of human-defined objectives, make predictions, recommendations, or decisions influencing real or virtual environments [9]. AI techniques encompass a large spectrum of approaches in terms of operational autonomy and accomplishable tasks. These include rule-based systems, expert systems, natural language processing, computer vision, and more [10].

ML is a subset of AI that focuses on developing algorithms enabling computers to learn from data and make predictions or take actions without explicit programming [11]. ML leverages large amounts of structured and unstructured data, employing multiple algorithms and techniques to learn from it and predict future outcomes. This is particularly valuable in fields like medicine, where decisions are complex and vary across individual patients. ML algorithms can continually improve their performance through experience, becoming more accurate over time [12]. They adapt and learn iteratively, using statistical models to identify patterns in data and draw useful inferences [13]. ML methodologies are diverse, including supervised, unsupervised and reinforcement learning approaches. [14]. For instance, supervised ML techniques train algorithms using labeled datasets to establish correlations. Notable examples of these methods encompass Support Vector Machines (SVM), Random Forest (RF), and Artificial Neural Networks (ANNs). It is worth noting that the distinction between supervised and unsupervised methods, although crisp from a theoretical perspective, has several practical applications. Indeed, the versatility of the above-mentioned algorithms makes them very effective in addressing specific tasks that involve unlabeled data. For instance, SVMs can also perform unsupervised clustering via one-class SVM. Similarly, RF can be adapted to perform unsupervised clustering and it is effective in the detection of anomalies or outliers in the raw data. ANNs are highly versatile by design and their field of application spans from supervised classification to unsupervised autoencoders and reinforcement deep Q-networks. In clinical applications, one of the major limitations of supervised ML is the availability of labeled data to be processed to properly train the system and build models for accurate predictions. Manual data labeling is time-consuming and often not practical in the clinical scenario. Furthermore, in case of uncommon diseases or clinical conditions, the labeling of a sufficiently large dataset is simply not feasible given the scarcity of data. In this scenario, transfer, semi-supervised and self-supervised learning are gaining popularity as techniques capable of overcoming the shortcomings of supervised and unsupervised approaches, trying to offer the best of both. Transfer learning is an ML technique in which the knowledge gained from a task is borrowed to boost the performance on a related task. Semi-supervised learning combines a small amount of labeled data with a larger set of unlabeled data, in a mixed supervised and unsupervised approach. A common semi-supervised technique combines clustering and classification algorithms: clustering groups unlabeled data based on similarity metrics and the labeled groups can subsequently be used to train a supervised model for classification. Self-supervised learning is an ML technique that does not require any labeled data and the model relies on the underlying structure of data to predict outcomes. The algorithm exploits inherent structures or relationships within the raw data to create meaningful training data, labeled without expert intervention.

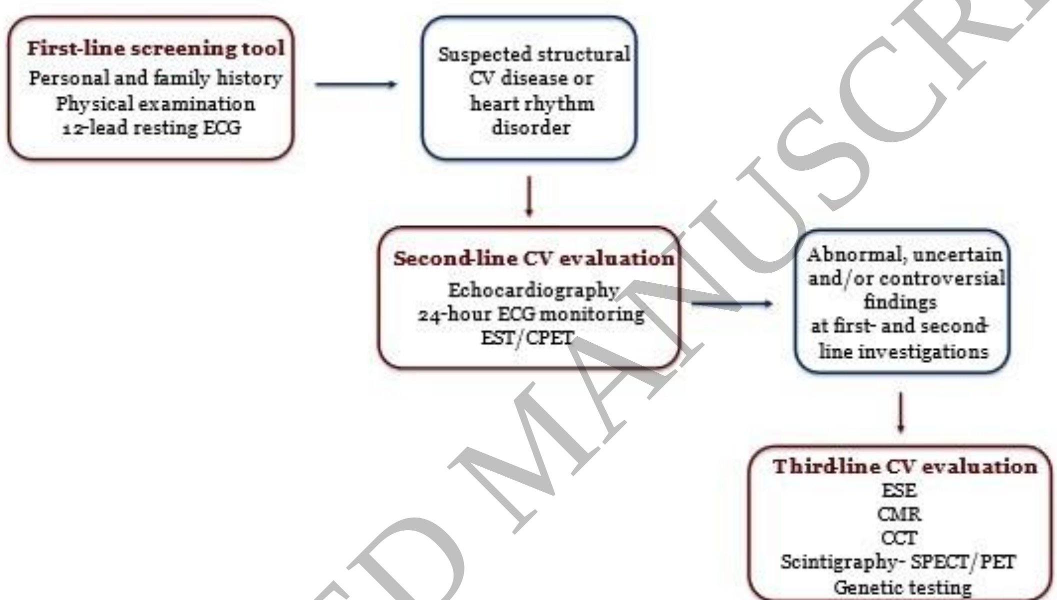
DL is a highly specialized class of ML, mainly composed of multi-layered ANNs. ANNs architecture was originally inspired by the structure and communication nodes and paths of the biological brain. The multi-layer architecture of ANNs (hence the term "deep") allows the extraction of increasingly higher-level features when transitioning from the raw input layer to the output layer. DL implies the training of ANNs with multiple layers to learn hierarchical representations of data. In other words, DL can uncover complex relationships that cannot be easily analyzed directly from raw input data by their representation in terms of mathematical models derived from principles, theories, or empirical observations. Unlike some traditional ML models that rely on manual feature extraction, DL models can directly process raw input data (e.g., images) and autonomously extract pertinent features. This capability has propelled DL to the forefront of AI applications, especially with the advent of powerful computational resources and the proliferation of big data [15]. While DL often requires more extensive training datasets, its application is context-dependent, excelling particularly in tasks like image recognition [16].

AI in Sports Cardiology

Cardiology has been at the forefront of examining AI technologies systematically [17]. ML, in particular, has proven to be valuable in interpreting CV imaging by integrating and correlating information from various sources to assist physicians in efficient interpretation [18]. In the field of cardiology, the initial applications of AI have focused on self-learning ANN applied to electrocardiography (ECG) [19]. Today, AI applications in cardiology are expanding to other areas, with few but promising results also in sports cardiology and the diagnosis of athlete's heart [20].

Numerous cardiovascular diagnostic techniques have been tested in athletes, but the optimal strategies for identifying key features of the athlete's heart remain unknown. A systematic approach to pre-participation screening (PPS) in athletes has been proposed, offering a step-by-step approach guided by the clinical scenario (Figure 3) [4]. AI has the potential to enhance PPS and sports cardiology by providing new tools and applications in each of these steps.

Figure 3. The step-by-step approach to athlete's heart [4]



ECG: electrocardiography; CV: cardiovascular; EST: exercise stress test; CPET: cardiopulmonary exercise test; ESE: exercise stress echocardiography; CMR: cardiac magnetic resonance; CCT: computed coronary tomography; SPECT: single photon emission computed tomography; PET: positron emission tomography.

Methods

To obtain the data needed to carry out the review, the Scopus and PubMed online electronic databases were searched to return the relevant literature. Some relevant terms about the use of AI-based CV diagnostic techniques in athletes were used to build a research key for the main topic of the study. Each database was searched according to its specific syntax rules. The literature returned from the searches was then reviewed and filtered by two authors, SP and MV, by the titles and abstracts, and then through full-text readings, which were carried out by EC, so that only the studies relevant to the review were included. Moreover, a manual search of published and unpublished studies (conference abstracts, textbooks, "grey" literature) was also conducted and reference lists of retrieved articles were screened.

1. History and physical examination

While modern diagnostic modalities have undoubtedly enhanced our diagnostic capabilities, history collection and physical examination remain indispensable components of the athlete's screening process [21]. AI may be used to augment the precision and efficacy of these conventional screening techniques.

Nowadays, several questionnaires are routinely used for the self-screening process of family and personal history of athletes [22], even if the medical supervision of the process is still essential [23]. The work by Rahman et al. [24] leveraged data from the American Heart Association questionnaire, using ML-based classifiers and information-based analysis to evaluate the questionnaire’s effectiveness. They employed three distinct models for this purpose: a SVM, a RF, and a naïve Bayes classifier. Their research yielded intriguing results, with the SVM demonstrating an accuracy of 0.742 in one experiment and the RF achieving 0.553 in another. However, the authors concluded that cardiologists using Electro- and Echo-cardiogram examinations are still more effective than these questionnaires alone in screening athletes.

The emergence of automated medical history-taking devices presents an exciting prospect. These tools not only streamline the data collection process but also assist physicians in pinpointing pivotal anamnestic details that might otherwise be overlooked during a conventional medical visit [25]. Recent advancements have seen the development of AI-driven automated medical history-taking devices [26,27]. These sophisticated tools double as clinical decision support systems, harnessing the power of ML algorithms to propose differential diagnoses. While current evidence suggests that these AI systems have yet to surpass human diagnostic acumen [28], and validation studies in athletes are still pending, their potential application in sports cardiology, especially in the realm of anamnestic data collection, is an exciting frontier to explore.

The physical examination of the athletes aims at identifying CV congenital abnormalities and features associated with genetic conditions such as Marfan syndrome [29]. Identifying and interpreting cardiac murmurs through auscultation is challenging, even for expert cardiologists, and the traditional classification of murmurs as "physiologic" or "pathologic" does not always differentiate for structural heart diseases that pose a risk of SCD [30]. AI can be utilized to improve the detection of valvular and congenital heart diseases through auscultation, employing a heart murmur detection algorithm [31]. A DL algorithm applied to recordings from a digital stethoscope has demonstrated the ability to detect cardiac murmurs, aortic stenosis, and mitral regurgitation with similar accuracy to that of an expert cardiologist [31,32]. Viviers et al. [33] focused on comparing the predictions made by a sports physician using a history questionnaire and physical examination to a technician using computer-assisted auscultation in determining the nature of cardiac murmurs in 131 collegiate athletes. Of the athletes, 25 were referred for further investigation based on murmurs, abnormal ECG, displaced apex, or possible Marfan syndrome. A cardiac ultrasound confirmed 3 cases of structural and 22 physiological murmurs. The computer-assisted auscultation showed higher sensitivity (100% vs 66.7%) but lower specificity (50% vs 66.7%) compared to the assessments made by a sports physician. This highlights the potential of computer-assisted auscultation as a feasible adjunct for improving the identification of structural murmurs in athletes; however, the over-referral by computer-assisted auscultation indicates a need for further investigation and possible refinements to the algorithm.

2. ECG

ECG is a widely used diagnostic technique in CV screening due to its simplicity, quickness, affordability, and non-invasiveness [34], even if the high false-positive rate is still one of the main criticisms raised [35]. Automated

ECG interpretation through digital ECG machines has become nearly universal and ECG analysis is the most developed application of ML methods in cardiology.

ML models can identify important features of the ECG, such as the P and T waves, QRS complexes, heart rate (HR), cardiac axis, various interval lengths, ST-changes, and common rhythm abnormalities like atrial fibrillation (AF) [36]. Large sets of digital ECGs linked to rich clinical data have been used to develop AI models for the detection of left ventricular (LV) dysfunction, silent AF and hypertrophic cardiomyopathy (HCM) [37]

Interpreting ECGs in athletes can be challenging because they often exhibit unique ECG patterns that differ from those seen in non-athletes [38]. These patterns can be mistakenly classified as abnormalities, leading to unnecessary testing and interventions. While numerous studies have validated the use of ML and DL techniques for identifying ECG patterns of CV diseases in the general population, these conditions, including s: ventricular arrhythmias [39], myocardial infarction [40] [41], HCM [42], dilated cardiomyopathy (DCM) [43], arrhythmogenic right ventricular cardiomyopathy (ARVC) [44], Brugada syndrome [45], Long QT syndrome (LQT) [46] and Wolff-Parkinson-White syndrome [47], bear significant relevance for sports physicians during pre-participation screenings of athletes.

Adetiba et al. [48] applied ANN to classify whether an athlete's ECG is normal or exhibits specific defects like tachyarrhythmia, bradyarrhythmia, or HCM. The authors extracted ECG signals, applied statistical signal processing techniques, and used the features as inputs to train the ANN to reach an overall accuracy of 90%. In a subsequent study from the same authors [49], published two years later, they revisited the same classification task. This time, however, the data was sourced from a novel wearable jersey they had designed. The results were even more promising, with the ANN achieving an accuracy of 100%. Differently, Lombardi et al. [50] used linear discriminant analysis to determine whether recreational athletes with idiopathic ventricular arrhythmias with a left bundle branch block and inferior axis morphology arrhythmia originated from the aortic sinus cusps or the right ventricular outflow tract. Manually extracted features from multiple modalities were used to create the linear separation between the two classes, achieving a final accuracy of 94.7%. Długosz et al. [51] embarked on a multifaceted study with two primary objectives: to estimate the level of cardiac troponin (cTnI) in amateur athletes using ECGs and to detect the presence of coronary artery disease (CAD) within the same group. The athletes' cTnI levels were meticulously recorded at multiple intervals, both before and after a sporting event. Interestingly, CAD was confirmed in six of the athletes. While their attempt to train a logistic regression model to estimate cTnI levels did not yield the desired results, their efforts to detect CAD were more fruitful. By employing a grid search-optimized decision tree and leveraging pre-extracted features from the athletes' ECGs, along with tabular records such as body mass index, age, and cTnI blood levels, they achieved commendable results. The best-performing model demonstrated an area under the curve (AUC) of 0.91, underscoring the potential of ML in enhancing ECG interpretation.

The advancement of high-performance computer and DL technologies has enabled the construction of models that detect diseases, predict outcomes, and automate measurements using raw ECG voltage data [52]. Several DL models have shown the ability to perform tasks beyond that of expert ECG operators [53]. This could be a promising field for the development of future studies specifically focused on athletes and the detection of SCD-related CV conditions.

Other ECG-based diagnostic modalities can be used to evaluate athletes: exercise stress test (EST), 24-hour Holter ECG monitoring and cardiopulmonary exercise test (CPET). ML-based techniques have been used to improve the diagnostic performance of EST in detecting CAD [47] and to identify major heart rhythm disorders in the 24-hour ECG monitoring [54] of the general population. Qammar et al. [55] ventured into the realm of EST with a unique approach. They employed ML algorithms to monitor and assess blood pressure variations during EST in a cohort of physically active individuals. The authors provided valuable insights into the subtle variations in cardiovascular response to stress tests between individuals with normal and high blood pressure. They highlighted the importance of load phase data and developed a classification algorithm based on statistical analysis of slope coefficients.

Finally, a growing body of research is focusing on the automatic detection of exercise thresholds in CPET [56]. Identifying these thresholds is crucial as they provide insights into an athlete's exercise tolerance and potential limitations, thus offering a future field for studies in active populations.

3. Echocardiography

Echocardiography is a valuable second-line diagnostic modality when there is suspicion of a structural cardiovascular disease during the initial step of athlete PPS [2]. However, interpreting echocardiograms can be challenging due to the technique's reliance on the operator, leading to potential errors in image acquisition and interpretation, resulting in inaccurate diagnoses and significant consequences for athletes. While ML in echocardiography is still in its early stages compared to its role in ECG, AI-based techniques can potentially increase the diagnostic role of this technique by providing complementary tools that generate accurate, consistent, and automated interpretations of echocardiograms [57]. This could reduce the risk of human error [6], as ML algorithms can analyze each pixel and its relationship with others, in addition to considering associated clinical metadata [58] [59].

DL techniques can efficiently evaluate nearly all structures and conditions relevant to a comprehensive echocardiographic evaluation of athletes [60], encompassing numerous potentially dangerous cardiovascular conditions, such as cardiomyopathy [61], valvular diseases [62] [63], aortic root diseases [64], pericardial effusion [65] and congenital heart diseases [66]. While there are not many studies specifically evaluating these conditions in athletes, they represent a key aim for the scientific community. These conditions are critical for sports physicians to recognize during athlete screenings due to their potential impact on health and performance. However, there is still a gap in the literature regarding ML-based techniques to accurately assess coronary artery origins, a crucial parameter in the echocardiographic evaluation of athletes [67].

Athletes may exhibit echocardiographic changes in cardiac structure and function that differ from those observed in sedentary individuals, making it challenging to differentiate between normal and abnormal findings [68] [69]. AI algorithms have the potential to identify these distinctive echocardiographic patterns and assist physicians in the differential diagnosis within the grey zones of athlete's heart [70], such as in the case of differential diagnosis of LV hypertrophy etiology [71]. Huang et al. [72] conducted a study utilizing unsupervised clustering to explore the validity of sport-specific adaptations in athletes' hearts. The study had two objectives: to identify athlete groups with similar characteristics by exploring the natural clustering of echocardiographic variables, and to evaluate the validity of sport-specific adaptation through a data-driven approach for assessing athlete's heart. They successfully demonstrated clear training-related adaptations among the groups defined by using Mitchell's classification. Furthermore, through agglomerative hierarchical clustering, two distinct clusters were identified for male and female athletes, confirming sport-specific adaptations. Narula et al. [73] investigated the diagnostic value of an ML framework incorporating speckle-tracking echocardiographic data for automated discrimination between HCM and physiological hypertrophy observed in athletes with a sensitivity and specificity of 87% and 82%, respectively. Additionally, Hwang et al. [71], recently validated a DL algorithm for the differential diagnosis of common left ventricular hypertrophy etiologies (hypertensive heart disease, HCM, and cardiac amyloidosis), using standard echocardiographic images from a cohort of 930 subjects. The algorithm, which employed a convolutional neural network-long short-term memory (CNN-LSTM) model, independently classified the three diagnoses on each of five standard echocardiographic views. The overall diagnostic accuracy was significantly higher at 92.3% compared to echocardiography specialists at 80.0% and 80.6%. These results suggest that DL can significantly enhance the diagnostic process in distinguishing between common etiologies of LV hypertrophy, offering a robust tool in the challenging differentiation of physiological adaptations in an athlete's heart from pathological conditions.

Finally, automated analysis of ESE is possible, as shown by a recent study [74], highlighting promising results in this third-line diagnostic technique in the athlete's heart diagnosis, often useful in suspicious of myocardial ischemia in master athletes [4].

4. Third-line cardiovascular evaluation

In situations where abnormal, uncertain, or controversial findings arise during the initial and second-line diagnostic evaluations, additional CV diagnostic modalities can be valuable in distinguishing between physiological adaptation and CV diseases in athletes [4].

4.1 Cardiac Magnetic Resonance

Cardiac Magnetic Resonance (CMR) is an established imaging modality for cardiovascular assessment in athletes, serving as the contemporary gold standard for evaluating myocardial structure and tissue architecture [75] [76]. Interpreting CMR images accurately is challenging, and errors can have significant consequences, also for athletes. Integrating ML into CMR can enhance efficiency and improve interpretation accuracy [76]. AI solutions have been proposed to facilitate image acquisition, reconstruction, and quality improvement, simplifying the CMR process [77] [78].

AI-based CMR analysis has been explored in the field of differential diagnosis between cardiac phenotypes [79] [80] [80]. A research by Bernardino et al. [81] utilized a linear statistical shape analysis framework to identify shape patterns indicating cardiac remodeling in athletes: they found that 89 triathletes had an increase in ventricular volumes and myocardial mass compared to 77 controls. They presented a linear statistical shape analysis framework that looked for shape differences between the athletes and a set of control participants. Their innovative approach combined dimensionality reduction techniques, principal component analysis, and partial least squares to provide a visual representation of cardiac changes due to endurance exercise. Logistic regression was then used to classify what shape patterns were the most discriminating between the two populations, and then they used this information to provide a visual representation of the changes. This framework was applied to CMR imaging for the study population which was able to highlight areas of the heart that undergo cardiac remodelling due to endurance exercise.

The emerging field of radiomics, involving the extraction of quantitative imaging features from digital medical images, has also gained interest [82]. Radiomics shows potential in discriminating between hypertensive heart disease and some CV diseases, such as HCM [83][84] This holds promise, especially in addressing ambiguous diagnostic scenarios ("grey zones") frequently encountered in athletes, even if, nowadays, there are no specific validation studies in athletes.

4.2 Coronary computed tomography and nuclear cardiac studies

To date, no specific studies regarding coronary computed tomography (CCT), single-photon emission computed tomography (SPECT) and positron emission tomography (PET) have been yet performed on athletes. However, there are some potential areas where AI-based techniques can increase the role of these 3rd-line sports cardiology diagnostic modalities.

Depending on local availability and expertise, CCT may be considered in athletes with symptoms suggestive of CAD or older, asymptomatic athletes with risk factors for CV disease or equivocal EST [85]. The integration of AI in CCT has the potential to reduce radiation dose while maintaining image quality. AI can also assist in CCT reporting, evaluating the burden of CAD, assessing myocardial ischemia, and predicting prognosis. Furthermore, AI can contribute to improving the process of coronary artery calcium scoring, an important indicator of atherosclerosis [86] [88].

4.3 Genetic testing

In recent years, the diagnostic role of genetic testing has gained attention [87] [88], particularly in individuals who exhibit an overlapping phenotype between inherited cardiac disease and athlete's heart [89] [90].

Recent advancements and emerging technologies in AI, along with the increasing availability of next-generation sequencing, offer researchers unprecedented possibilities for dynamic and complex genomic analyses [91]. By combining these technologies, a deeper understanding of heterogeneous polygenic CV diseases, improved prognostic guidance, and ultimately greater personalized medicine can be achieved. SVM models have been used to predict polygenic risk factors for hypertension [92] or inherited arrhythmias [93], while ANN models have been used to predict advanced coronary artery calcium [94] and inheritable DCM [95], even if, to date, no specific studies have been conducted in athletes

With advancements in sequencing technologies, whole exome and genome sequencing have become more accessible and can provide comprehensive genetic information [88]. These techniques enable the identification of rare genetic variants and novel gene-disease associations that may potentially contribute to cardiac conditions in athletes. Integrating these genetic findings with functional studies and clinical data can shed light on the pathogenic mechanisms underlying these disorders.

In addition, the application of ML algorithms in the analysis of genetic data can aid in interpreting and predicting disease outcomes. Training AI models on large-scale genomic datasets could make it possible to identify genetic patterns, biomarkers, and disease subtypes that can inform risk stratification and personalized treatment approaches, as well as for athletes [91].

Wearable devices in sports cardiology

CV wearables, including HR monitors and activity trackers, are gaining great interest in the sports medicine field. These devices are designed to track physical activity, estimate the steps, energy expenditure and intensity levels achieved, and provide insights into general health and well-being. Indeed, incorporating HR data from wearables can guide training intensity, making it helpful in designing training regimens for athletes and personalized exercise prescriptions for patients with cardiac conditions [96] [97] [98,99].

The integration of AI into wearable devices using deep neural networks (DNNs) is progressively making them suitable for real-time, on-person health monitoring [100] [101]. Wearables equipped with ML models can assess other vital signs, such as blood pressure, respiratory rate, and oxygen saturation, allowing for comprehensive cardiovascular evaluation during exercise and recovery periods [102].

Sensor development has allowed HR monitoring to evolve into a surface electrode for ECG recording. While not a replacement for clinical outpatient monitoring, these advances can help identify major arrhythmias, especially AF [103–105]. The AppleWatch©, for example, has shown excellent detection ability for AF [106]. It utilizes a single-lead ECG and a photoplethysmography (PPG) sensor to measure cardiac conduction and blood flow changes [107], respectively, enabling the detection of sinus rhythm, AF, and inconclusive rhythms with high sensitivity [106] [108]. The implementation of AI in wearables can have great potential in risk stratification of athletes, being helpful in some high-risk CV conditions, such as LQT [109] [110] or ST-segment elevation [111], even if there are no validations studies in sportsmen, yet [112] Indeed, false positives and movement artifacts during intense physical activity are potential criticisms to their application [114].

Peritz et al. [113] showed how handheld smartphone ECG monitors could represent a helpful tool connecting the athletic trainer to the physician for the real-time detection of potentially fatal arrhythmias. Castillo-Atoche et al. [114] utilized a dataset of more than 50000 ECG samples from 487 patients to predict arrhythmias in athletes in real-time. The samples were analyzed, with a majority (55222 samples from 480 subjects) used for training the model and a smaller subset (1320 samples from 7 athletes) reserved for testing. The training dataset was an amalgamation of several open-access online datasets, while the test set was derived from manual readings from the wearable under discussion. The CNN model employed in the study demonstrated an accuracy of 94.3% on the training set. Furthermore, the model's performance on the test set averaged an accuracy of 93.9% across the seven athletes. Moreover, Green et al. [115] theorized that patients with obstructive HCM could be distinguished from controls using a combination of ML and the PPG capabilities of a commercial biosensor: this holds great potential applications also in athletes [116] [118].

Recently, nanomaterial-based sensors have garnered increased attention due to their interaction with the human body. These materials can be attached to clothing or applied directly on the skin for real-time monitoring of various physical, chemical, biological, and environmental signals, thus making them potentially useful for sports-related applications [117]. Such developments can enable the measurement of biochemical markers, also related to physical activity [117].

Integration of wearables with mobile applications and cloud-based platforms facilitates seamless data sharing and collaboration between athletes, coaches, and healthcare professionals, enabling remote monitoring and optimizing training regimens based on personalized data-driven insights. As sensor technologies advance and their adoption increases, physicians should recognize their utility, evaluate their potential and limitations, and ensure their appropriate use in clinical practice [118] [119]. This includes being mindful of the balance between sensitivity and specificity, particularly in the context of athletic performance and exercise, to minimize the risk of false positives and ensure accurate and reliable health monitoring.

Ethical dilemmas

Despite its potential benefits, AI is still relatively new and unfamiliar, which gives rise to various ethical and legal dilemmas that must be addressed [120]. From an ethical standpoint, considerations such as informed consent, safety, transparency, algorithmic fairness, biases, and data privacy need to be carefully examined; access to highly specialized state-of-the-art technology, not normally accessible to everyone, must also be considered. Legally, factors such as safety and effectiveness, liability, data protection, privacy, cybersecurity, and intellectual property rights come into play.

Furthermore, it is important to acknowledge the potential flaws in designing and implementing AI-driven studies. Many studies reporting AI applications have retrospective designs and small sample sizes, raising concerns about generalizability. Moreover, there is a risk of selection bias in AI-driven studies, including sampling and observer bias. It is also crucial to recognize that AI-driven technologies may replicate and amplify existing patterns of marginalization, inequality, and discrimination that exist within the analyzed populations. The features and biases of the data chosen to train the algorithms can influence the outcomes and perpetuate the preconceptions and biases of the investigators [121].

As AI becomes more advanced, it becomes less comprehensible to humans, even to the engineers and data scientists who created the algorithms. In safety-critical situations like medicine, the lack of transparency in these techniques can lead to incorrect decision-making and pose risks to human life. Explainable AI (XAI) development aims to make AI algorithms more interpretable, allowing humans to understand how they work, trust their results, identify potential biases, and assess their accuracy and transparency [122,123]. Implementing XAI ensures that AI systems meet regulatory standards, adhere to good practices, and can be deployed more efficiently in high-risk domains such as the medical field [124].

The increasing use of smart medical devices and AI-driven digital health applications raises concerns about the dehumanization of medicine [76]. Intelligent applications are increasingly replacing certain aspects of physicians' work in various sectors. However, the question of trust arises when decision-makers may not fully understand the AI system they are relying on. Ultimately, when there is a conflict in management plans, physicians should have the final and most important word when it comes to AI-driven decision-making in the medical field [76], and also in the sports cardiology evaluation of athletes. Striking a balance is crucial to maintaining a healthy physician-athlete relationship, integrating AI technologies when necessary to alleviate administrative burdens [125].

Considerations and future directions

The application of AI in sports cardiology is still in its infancy, and few studies have been conducted specifically in athletes (Table 1). Even if some of them are only proposals of AI-based methodologies [55,126,127], nearly a few have provided comparative data [128,129], and most of them have methodological flaws (Table 2) [130], their initial findings are promising.

Table 1. Summary of studies analyzing various AI-based cardiovascular diagnostic techniques in athletes

Step-by-step approach	CV diagnostic method	Study	Sample size	AI-based method	Problem addressed	Performance metric of the AI-based method	Comparison
First-line screening tool	Anamnesis	Rahman et al., 2013 [24]	470	- naïve Bayes - SVM - RF	Determine whether the AHA screening questionnaire correctly screens athletes if compared with ECG and ECHO	Accuracy– RF = 0.553	NA
	Auscultation	Viviers et al., 2017 [128]	131	Computer-assisted auscultation system	Determine whether a computer-assisted auscultation system has the ability to detect the presence of structural murmur if compared with a sports physician auscultation	Computer-assisted auscultation system – sensitivity = 100%, specificity = 50%	Physician auscultation – sensitivity 66.7%, specificity 66.7%
	ECG	Długosz et al., 2018 [51]	160	- DT - LR	- Use ECGs to estimate the level of cTNI in amateur athletes - Detect CAD in athletes	CAD detection - AUC = 0.91	NA
		Lombardi et al., 2018 [50]	26	Linear discriminant analysis	Determine whether patients with idiopathic ventricular arrhythmias with left bundle branch block and inferior axis morphology arrhythmia originated from the aortic sinus cusps or the right ventricular outflow tract	Accuracy = 0.947	NA
		Adetiba et al., 2017 [131]	40	ANN	Automatic heart defect detection (tachyarrhythmia,brad	Accuracy = 0.9	NA

					yarrhythmia and HCM) for athletes		
	ECG (wereables)	Adetiba et al., 2019 [49]	40	ANN	Develop a wearable-ECG that can be worn by athletes to help automatically detect defects	Accuracy = 1	NA
		Castillo Atoche et al., 2022 [132]	56542 samples from 487 patients	CNN	Automatically detect arrhythmias in athletes in real time	Accuracy = 0.939	NA
Second-line CV evaluation	EST	Qammar et al., 2022 [55]	19	ML algorithms	Correctly classify BP during EST in active population	NA	NA
	ECHO	Narula et al., 2016 [73]	77 athletes and 62 HCM patients	- SVM - RF - ANN	Investigate the diagnostic value of a ML framework that incorporates speckle-tracking echocardiographic data for automated discrimination of HCM from physiological hypertrophy in athletes	Sensitivity = 96%, specificity = 77%	E/A (sensitivty = 79%, specificity = 77%), e' (sensitivity = 86%, specificity = 82%), longitudinal strain (sensitivity = 68%, specificity = 77%)
		Huang et al., 2022 [72]	598	- Agglomerative hierarchical Clustering - Multiple	- Identify athlete groups with similar characteristics - Investigate the validity of sport-specific adaption for evaluating	NA	NA

				regression analysis	athlete's hearts		
Third-line CV evaluation	CMR	Bernardino et al., 2020 [81] [NO_PRINTED_FORM]	77 controls and 89 athletes	- Logistic regression - Principal component analysis - Statistical shape analysis	Highlight areas of the heart that undergo cardiac remodelling due to endurance exercise	NA	NA
Full-CV risk of athlete	Anthropometric data + demographic data + biomedical data + ECG	Barbieri et al., 2020 [133]	26002	- DT - Logistic regression	Classify whether an athlete is at cardiovascular risk or not	AUC = 0.78	NA

ANN: automatic neural network; AUC: area under the curve; BP: blood pressure; CAD: coronary artery disease; CMR: cardiac magnetic resonance; CNN: convolutional neural network; cTNI: cardiac troponin; DT: decision tree; ECG: electrocardiogram; ECHO: echocardiography; EST: exercise stress test; HCM: hypertrophic cardiomyopathy; LR: logistic regression; ML: machine learning; NA: not available; RF: random forest; SVM: support vector machine.

Table 2. Evaluation of methodology of included studies

Study	RISK OF BIAS				APPLICABILITY CONCERNS		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Rahman et al., 2013 [24]	☺	☺	☺	?	☺	☺	☺
Viviers et al., 2017 [128]	☹	☺	☹	☹	☹	☺	☹
Długosz et al., 2018 [51]	☹	☹	☺	☺	☹	☹	☺
Lombardi et al., 2018 [50]	☹	☺	☺	☹	☹	☹	☺
Adetiba et al., 2017 [131]	☹	☺	☺	?	☺	☹	☺
Adetiba et al., 2019 [49]	☹	?	☹	?	?	?	☹
Castillo Atoche et al., 2022 [132]	☹	?	☹	☹	☹	?	☹
Qammar et al., 2022 [55]	☹	☺	☹	☺	☺	?	☹
Narula et al., 2016 [129]	☹	☺	☺	☹	☺	☺	☺
Huang et al., 2022 [126]	☺	☺	☹	☹	☺	☺	☹
Bernardino et al., 2020 [127]	☹	☺	☺	?	☹	☹	☺
Barbieri et al., 2020 [133]	☺	☺	☺	?	☺	☺	☺

☺ Low Risk ☹ High Risk ? Unclear Risk

AI algorithms can also analyze large volumes of data to identify patterns and relationships that may go unnoticed with traditional analysis methods. The data miming is thus defined as the process of discovering meaningful patterns in data, that can be advantageous somehow for the user [84]. As the amount of collected data has increased, researchers and physicians are interested in evaluating their diagnostic value using data miming, and eventually suggest that the observed variables may be changed or increased to support medical decisions. Several data miming methods have already been used as decision support systems for medical diagnosis [134], and these methods may be applied to large datasets to estimate health risk. The PPS and the diagnosis of athlete's heart may be promising fields in that sense, given the fact that the step-by-step approach may offer a great amount of CV data to the physician evaluating an athlete. For instance, Barbieri et al. [133] utilized a resampling technique to enhance the assessment of CV risk in athletes, especially when dealing with imbalanced data. Using data from over 25000 athletes, their decision tree model demonstrated promising results in terms of the AUC and sensitivity. Although the study lacked a comparison data set, its findings suggest the potential to improve CV risk assessment in athletes, refining clinical decision-making, and reducing unnecessary examinations. However, these studies are often limited in size and scope, leading to potential biases. There is a pressing need for larger-scale, diverse studies to validate these methods and understand the limits of AI prediction accuracy. These are useful results in the field of sports cardiology give rise to hope for the future. As the field progresses, there's hope for a future where a multi-modality set of data can be analyzed collectively to minimize the risk of SCD in athletes. One of the great future goals could be the creation of a model predicting the overall risk of adverse events in athletes capable of integrating all screening and diagnostic methods implemented from first to third-line investigations (Figure 4). However, it is crucial to critically evaluate the number of subjects required to train such algorithms, especially for detecting severe diseases with low prevalence in a young, multi-ethnic, and predominantly healthy population like athletes. The need for substantial datasets to achieve precision and avoid overdiagnosis, which can lead to distress and unnecessary testing, cannot be overstated. This tool would not replace clinical decision-making but would help in risk stratification and the most appropriate choice for the athlete's safety. Moreover, the potential of AI doesn't stop at diagnosis. With advancements in wearable technology and real-time data monitoring, AI can be instrumental in continuous health monitoring, early detection of anomalies, and even in predicting potential health risks based on an athlete's health data trends.

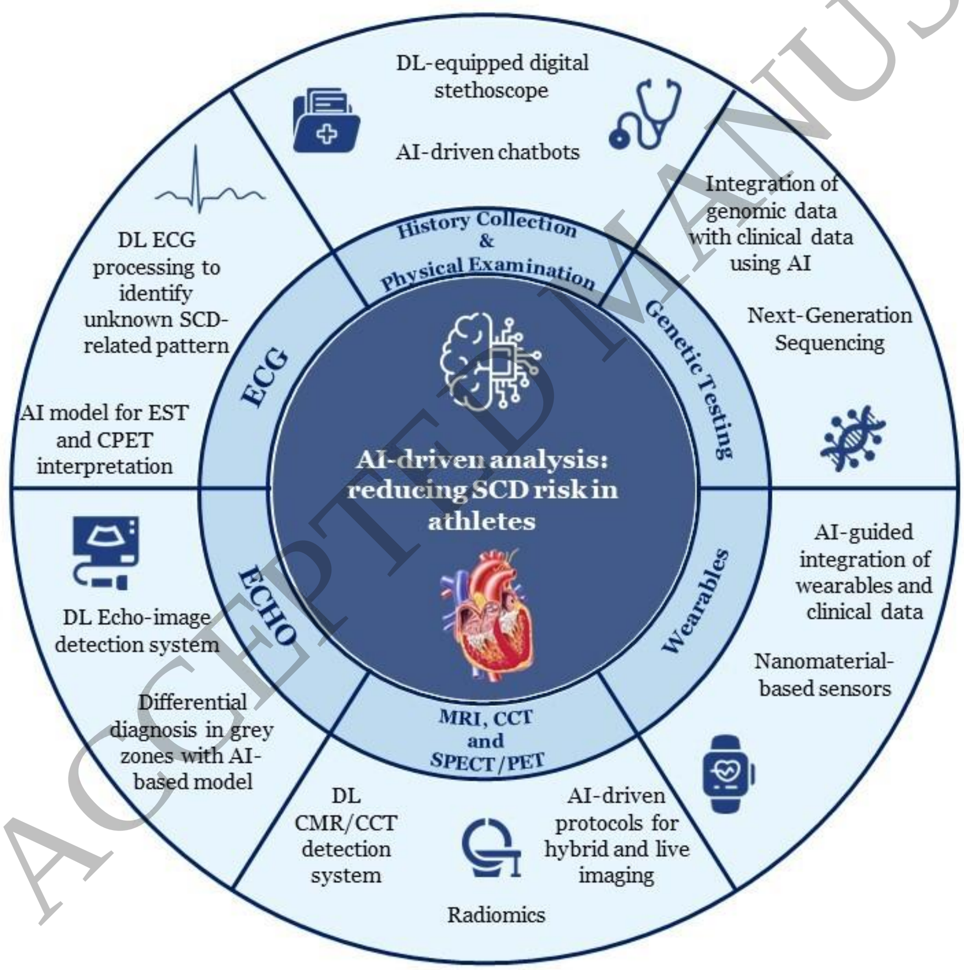
However, for AI to be fully integrated and accepted in sports cardiology:

1. Validation and Standardization: More studies with larger sample sizes and valid comparison groups are needed to validate the efficacy of AI models. Standardized protocols for data collection, processing, and analysis should be established to ensure consistency and reliability across studies.
2. Interdisciplinary Collaboration: Collaboration between cardiologists, sports scientists, data scientists, and AI experts will be crucial. Such interdisciplinary teams can ensure that AI models are both medically sound and technologically advanced.
3. Ethical Considerations: As with all AI applications in healthcare, ethical considerations, especially concerning data privacy and security, will be paramount. Ensuring that athletes' data is protected and used responsibly will be crucial for the widespread adoption of AI in sports cardiology.

4. Education and Training: For AI to be effectively used in clinical settings, healthcare professionals need to be educated and trained on these technologies. This will ensure that they can interpret AI findings correctly and integrate them into their clinical decision-making process.

5. Patient-Centered Approach: While AI can provide valuable insights, the final decision should always consider the athlete's unique circumstances, preferences, and values. AI should be used as a tool to aid decision-making, not replace it.

Figure 4. The potential use of AI in sports cardiology



CV: cardiovascular; DL: deep learning; CMR: cardiac magnetic resonance; CCT: computed coronary tomography;

SCD: sudden cardiac death; AI: artificial intelligence; EST: exercise stress test; ECG: electrocardiography; PPS: pre-participation screening; ECHO: echocardiography

Conclusions

In conclusion, integrating AI into sports cardiology holds many potential applications for advancing the evaluation and care of athletes' hearts. AI technologies, such as ML and offer opportunities for improved risk stratification, diagnosis, treatment planning, and monitoring in this specialized field. From imaging techniques to genetic testing, through new wearable devices, AI has the potential to positively influence the sports cardiology practice. However, careful attention must be given to ethical and legal dilemmas, ensuring transparency, fairness, and privacy in the implementation of AI. A balanced approach that combines the expertise of physicians with the power of AI technologies will lead to enhanced patient care, better outcomes, and a deeper understanding of the complex CV health of athletes. As AI continues to evolve, research, collaboration, and regulatory frameworks will be essential to unlock the full potential of this transformative technology in sports cardiology.

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References

1. D'Ascenzi F, Valentini F, Pistoresi S *et al.* Causes of sudden cardiac death in young athletes and non-athletes: systematic review and meta-analysis: Sudden cardiac death in the young. *Trends Cardiovasc Med* 2022;**32**:299–308.

2. Palermi S, Serio A, Vecchiato M *et al.* Potential role of an athlete-focused echocardiogram in sports eligibility. *World J Cardiol* 2021;**13**:271–97.

3. D'Andrea A, Sperlongano S, Russo V *et al.* The Role of Multimodality Imaging in Athlete's Heart Diagnosis: Current Status and Future Directions. *J Clin Med* 2021;**10**, DOI: 10.3390/jcm10215126.

4. Palermi S, Cavarretta E, Ascenzi FD *et al.* Athlete ' s Heart : A Cardiovascular Step-By-Step Multimodality Approach. 2023;**24**.

5. Chang AC. Primary prevention of sudden cardiac death of the young athlete: the controversy about the screening electrocardiogram and its innovative artificial intelligence solution. *Pediatr Cardiol* 2012;**33**:428–33.

6. Itchhaporia D. Artificial intelligence in cardiology. *Trends Cardiovasc Med* 2022;**32**:34–41.

7. Choi RY, Coyner AS, Kalpathy-Cramer J *et al.* Introduction to Machine Learning, Neural Networks, and Deep Learning. *Transl Vis Sci Technol* 2020;**9**:14.

8. World Health Organization. Ethics and Governance of Artificial Intelligence for Health: WHO guidance. *World Health Organization* 2021:1–148.

9. Artificial Intelligence in Society. *Artificial Intelligence in Society* 2019, DOI: 10.1787/EEDFEE77-EN.

10. How to edit anthropomorphic language about artificial intelligence. *Nature Reviews Physics 2023 5:5* 2023;**5**:263–263.

11. Sardar P, Abbott JD, Kundu A *et al.* Impact of Artificial Intelligence on Interventional Cardiology: From Decision-Making Aid to Advanced Interventional Procedure Assistance. *JACC Cardiovasc Interv* 2019;**12**:1293–303.

12. Patel B, Makaryus AN. Artificial Intelligence Advances in the World of Cardiovascular Imaging. *Healthcare (Switzerland)* 2022;**10**:1–11.

13. Pettit RW, Fullem R, Cheng C *et al.* Artificial intelligence, machine learning, and deep learning for clinical outcome prediction. *Emerg Top Life Sci* 2021;**5**:729–45.

14. Petersen SE, Abdulkareem M, Leiner T. Artificial Intelligence Will Transform Cardiac Imaging—Opportunities and Challenges. *Front Cardiovasc Med* 2019;**6**:1–6.

15. Weng SF, Reps J, Kai J *et al.* Can machine-learning improve cardiovascular risk prediction using routine clinical data? *PLoS One* 2017;**12**:e0174944.

16. Krittanawong C, Zhang H, Wang Z *et al.* Artificial Intelligence in Precision Cardiovascular Medicine. *J Am Coll Cardiol* 2017;**69**:2657–64.

17. Seetharam K, Shrestha S, Sengupta PP. Artificial Intelligence in Cardiovascular Medicine. *Curr Treat Options Cardiovasc Med* 2019;**21**:25.

18. Seetharam K, Brito D, Farjo PD *et al.* The Role of Artificial Intelligence in Cardiovascular Imaging: State of the Art Review. *Front Cardiovasc Med* 2020;**7**:618849.

19. Dassen WR, Mulleneers R, Smeets J *et al.* Self-learning neural networks in electrocardiography. *J Electrocardiol* 1990;**23 Suppl**:200–2.

20. Bellfield RAA, Ortega-Martorell S, Lip GYH *et al.* The Athlete's Heart and Machine Learning: A Review of Current Implementations and Gaps for Future Research. *J Cardiovasc Dev Dis* 2022;**9**, DOI: 10.3390/jcdd9110382.

21. Rossoni A, Vecchiato M, Brugin E *et al.* The eSports Medicine: Pre-Participation Screening and Injuries Management-An Update. *Sports (Basel)* 2023;**11**, DOI: 10.3390/sports11020034.

22. Maron BJ, Thompson PD, Puffer JC *et al.* Cardiovascular preparticipation screening of competitive athletes. A statement for health professionals from the Sudden Death Committee (clinical cardiology) and Congenital Cardiac Defects Committee (cardiovascular disease in the young), American Heart Association. *Circulation* 1996;**94**:850–6.

23. Palermi S, Sirico F, Fernando F *et al.* Limited diagnostic value of questionnaire-based pre-participation screening algorithms: a “risk-exposed” approach to sports activity. *J Basic Clin Physiol Pharmacol* 2022;**33**:655–63.

24. Rahman QA, Kanagalingam S, Pinheiro A *et al.* What we found on our way to building a classifier: A critical analysis of the AHA screening questionnaire. *Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)* 2013;**8211 LNAI**:225–36.

25. Benaroia M, Elinson R, Zarnke K. Patient-directed intelligent and interactive computer medical history-gathering systems: a utility and feasibility study in the emergency department. *Int J Med Inform* 2007;**76**:283–8.

26. Singhal K, Azizi S, Tu T *et al.* Large Language Models Encode Clinical Knowledge. 2022:1–44.

27. Harada Y, Shimizu T. Impact of a Commercial Artificial Intelligence–Driven Patient Self-Assessment Solution on Waiting Times at General Internal Medicine Outpatient Departments: Retrospective Study. *JMIR Med Inform* 2020;**8**, DOI: 10.2196/21056.

28. Kelly CJ, Karthikesalingam A, Suleyman M *et al.* Key challenges for delivering clinical impact with artificial intelligence. *BMC Med* 2019;**17**:1–9.

29. Giese EA, O’Connor FG, Brennan FH *et al.* The athletic preparticipation evaluation: cardiovascular assessment. *Am Fam Physician* 2007;**75**:1008–14.

30. Austin A V, Owens DS, Prutkin JM *et al.* Do “pathologic” cardiac murmurs in adolescents identify structural heart disease? An evaluation of 15 141 active adolescents for conditions that put them at risk of sudden cardiac death. *Br J Sports Med* 2022;**56**:88–94.

31. Lim GB. AI used to detect cardiac murmurs. *Nat Rev Cardiol* 2021;**18**:460.

32. Thompson WR, Reinisch AJ, Unterberger MJ *et al.* Artificial Intelligence-Assisted Auscultation of Heart Murmurs: Validation by Virtual Clinical Trial. *Pediatr Cardiol* 2019;**40**:623–9.

33. Viviers PL, Kirby J-AH, Viljoen JT *et al.* The Diagnostic Utility of Computer-Assisted Auscultation for the Early Detection of Cardiac Murmurs of Structural Origin in the Periodic Health Evaluation. *Sports Health* 2017;**9**:341–5.

34. Myerburg RJ, Vetter VL. Electrocardiograms Should Be Included in Preparticipation Screening of Athletes. *Circulation* 2007;**116**:2616–26.

35. Baggish AL, Hutter AMJ, Wang F *et al.* Cardiovascular screening in college athletes with and without electrocardiography: A cross-sectional study. *Ann Intern Med* 2010;**152**:269–75.

36. Rajpurkar P, Hannun AY, Haghpanahi M *et al.* Cardiologist-Level Arrhythmia Detection with Convolutional Neural Networks. 2017.

37. Siontis KC, Noseworthy PA, Attia ZI *et al.* Artificial intelligence-enhanced electrocardiography in cardiovascular disease management. *Nat Rev Cardiol* 2021;**18**:465.

38. Baggish AL, Battle RW, Beaver TA *et al.* Recommendations on the Use of Multimodality Cardiovascular Imaging in Young Adult Competitive Athletes: A Report from the American Society of Echocardiography in Collaboration with the Society of Cardiovascular Computed Tomography and the Society for Car. *J Am Soc Echocardiogr* 2020;**33**:523–49.

39. Nakamura T, Nagata Y, Nitta G *et al.* Prediction of premature ventricular complex origins using artificial intelligence-enabled algorithms. *Cardiovasc Digit Health J* 2021;**2**:76–83.

40. Cho Y, Kwon J-M, Kim K-H *et al.* Artificial intelligence algorithm for detecting myocardial infarction using six-lead electrocardiography. *Sci Rep* 2020;**10**:20495.

41. Jurado IC, Fedjajevs A, Vanschoren J *et al.* Interpretable Assessment of ST-Segment Deviation in ECG Time Series. *Sensors (Basel)* 2022;**22**, DOI: 10.3390/S22134919.

42. Ko W-Y, Siontis KC, Attia ZI *et al.* Detection of Hypertrophic Cardiomyopathy Using a Convolutional Neural Network-Enabled Electrocardiogram. *J Am Coll Cardiol* 2020;**75**:722–33.

43. Shrivastava S, Cohen-Shelly M, Attia ZI *et al.* Artificial Intelligence-Enabled Electrocardiography to Screen Patients with Dilated Cardiomyopathy. *Am J Cardiol* 2021;**155**:121–7.

44. Papageorgiou VE, Zegkos T, Efthimiadis G *et al.* Analysis of digitalized ECG signals based on artificial intelligence and spectral analysis methods specialized in ARVC. *Int J Numer Method Biomed Eng* 2022;**38**:e3644.

45. Vozzi F, Dimitri GM, Piacenti M *et al.* Artificial intelligence algorithms for the recognition of Brugada type 1 pattern on standard 12-leads ECG. *EP Europace* 2022;**24**:euac053.558.

46. Bos JM, Attia ZI, Albert DE *et al.* Use of Artificial Intelligence and Deep Neural Networks in Evaluation of Patients With Electrocardiographically Concealed Long QT Syndrome From the Surface 12-Lead Electrocardiogram. *JAMA Cardiol* 2021;**6**:532–8.

47. Nishimori M, Kiuchi K, Nishimura K *et al.* Accessory pathway analysis using a multimodal deep learning model. *Sci Rep* 2021;**11**:8045.

48. Adetiba E, Iweanya VC, Popoola SI *et al.* Automated detection of heart defects in athletes based on electrocardiography and artificial neural network. *Cogent Eng* 2017;**4**, DOI: 10.1080/23311916.2017.1411220.

49. Adetiba E, Onosenema EN, Akande V *et al.* Development of an ECG Smart Jersey Based on Next Generation Computing for Automated Detection of Heart Defects Among Athletes. *Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)* 2019;**11466 LNBI**:524–33.

50. Lombardi G, Sorbo AR, Guida G *et al.* Magnetocardiographic classification and non-invasive electro-anatomical imaging of outflow tract ventricular arrhythmias in recreational sport activity practitioners. *J Electrocardiol* 2018;**51**:433–9.

51. Długosz D, Królak A, Eftestøl T *et al.* ECG signal analysis for troponin level assessment and coronary artery disease detection: The NEEDED study 2014. *Proceedings of the 2018 Federated Conference on Computer Science and Information Systems, FedCSIS 2018* 2018;**15**:1065–8.

52. Herman R, Demolder A, Vavrik B *et al.* Validation of an automated artificial intelligence system for 12-lead ECG interpretation. *J Electrocardiol* 2024;**82**:147–54.

53. Miura K, Yagi R, Miyama H *et al.* Deep learning-based model detects atrial septal defects from electrocardiography: a cross-sectional multicenter hospital-based study. *EClinicalMedicine* 2023;**63**, DOI: 10.1016/J.ECLINM.2023.102141.

54. Fiorina L, Maupain C, Gardella C *et al.* Evaluation of an Ambulatory ECG Analysis Platform Using Deep Neural Networks in Routine Clinical Practice. *J Am Heart Assoc* 2022;**11**:e026196.

55. Qammar NW, Orinaitė U, Šiaučiūnaitė V *et al.* The Complexity of the Arterial Blood Pressure Regulation during the Stress Test. *Diagnostics (Basel)* 2022;**12**, DOI: 10.3390/DIAGNOSTICS12051256.

56. Zignoli A. Machine Learning Models for the Automatic Detection of Exercise Thresholds in Cardiopulmonary Exercising Tests: From Regression to Generation to Explanation. *Sensors (Basel)* 2023;**23**, DOI: 10.3390/s23020826.

57. Alsharqi M, Woodward WJ, Mumith JA *et al.* Artificial intelligence and echocardiography. *Echo Res Pract* 2018;**5**:R115–25.

58. Barry T, Farina JM, Chao C-J *et al.* The Role of Artificial Intelligence in Echocardiography. *J Imaging* 2023;**9**, DOI: 10.3390/jimaging9020050.

59. Zhang J, Gajjala S, Agrawal P *et al.* Fully Automated Echocardiogram Interpretation in Clinical Practice. *Circulation* 2018;**138**:1623–35.

60. Donati F, Guicciardi C, Lodi E *et al.* Echocardiography in the preparticipation screening: an old topic revisited. *J Cardiovasc Med (Hagerstown)* 2023, DOI: 10.2459/JCM.0000000000001460.

61. Liu B, Chang H, Yang D *et al.* A deep learning framework assisted echocardiography with diagnosis, lesion localization, phenogrouping heterogeneous disease, and anomaly detection. *Sci Rep* 2023;**13**:3.

62. Playford D, Bordin E, Mohamad R *et al.* Enhanced Diagnosis of Severe Aortic Stenosis Using Artificial Intelligence: A Proof-of-Concept Study of 530,871 Echocardiograms. *JACC Cardiovasc Imaging* 2020;**13**:1087–90.

63. Moghaddasi H, Nourian S. Automatic assessment of mitral regurgitation severity based on extensive textural features on 2D echocardiography videos. *Comput Biol Med* 2016;**73**:47–55.

64. Karužas A, Balčiūnas J, Fukson M *et al.* Artificial intelligence for automated evaluation of aortic measurements in 2D echocardiography: Feasibility, accuracy, and reproducibility. *Echocardiography* 2022;**39**:1439–45.

65. Wu C, Cheng C, Chen H *et al.* Tien-Yu Chen 6 ,. 2022.

66. Truong VT, Nguyen BP, Nguyen-Vo T-H *et al.* Application of machine learning in screening for congenital heart diseases using fetal echocardiography. *Int J Cardiovasc Imaging* 2022, DOI: 10.1007/s10554-022-02566-3.

67. Bianco F, Colaneri M, Bucciarelli V *et al.* Echocardiographic screening for the anomalous aortic origin of coronary arteries. *Open Heart* 2021;**8**, DOI: 10.1136/openhrt-2020-001495.

68. Carbone A, D’Andrea A, Riegler L *et al.* Cardiac damage in athlete’s heart: When the “supernormal” heart fails! *World J Cardiol* 2017;**9**:470–80.

69. Niederseer D, Rossi VA, Kissel C *et al.* Role of echocardiography in screening and evaluation of athletes. *Heart* 2020, DOI: 10.1136/heartjnl-2020-317996.

70. D’Andrea A, Mele D, Palermi S *et al.* [Grey zones in cardiovascular adaptations to physical exercise: how to navigate in the echocardiographic evaluation of the athlete’s heart]. *G Ital Cardiol (Rome)* 2020;**21**:457–68.

71. Hwang I-C, Choi D, Choi Y-J *et al.* Differential diagnosis of common etiologies of left ventricular hypertrophy using a hybrid CNN-LSTM model. *Sci Rep* 2022;**12**:20998.

72. Huang K-C, Lin C-E, Lin L-Y *et al.* Data-driven clustering supports adaptive remodeling of athlete's hearts: An echocardiographic study from the Taipei Summer Universiade. *J Formos Med Assoc* 2022;**121**:1495–505.

73. Narula S, Shameer K, Salem Omar AM *et al.* Machine-Learning Algorithms to Automate Morphological and Functional Assessments in 2D Echocardiography. *J Am Coll Cardiol* 2016;**68**:2287–95.

74. Upton R, Mumith A, Beqiri A *et al.* Automated Echocardiographic Detection of Severe Coronary Artery Disease Using Artificial Intelligence. *JACC Cardiovasc Imaging* 2022;**15**:715–27.

75. Gati S, Sharma S, Pennell D. The Role of Cardiovascular Magnetic Resonance Imaging in the Assessment of Highly Trained Athletes. *JACC Cardiovasc Imaging* 2018;**11**:247–59.

76. Karatzia L, Aung N, Aksentijevic D. Artificial intelligence in cardiology: Hope for the future and power for the present. *Front Cardiovasc Med* 2022;**9**:945726.

77. Biasiolli L, Hann E, Lukaschuk E *et al.* Automated localization and quality control of the aorta in cine CMR can significantly accelerate processing of the UK Biobank population data. *PLoS One* 2019;**14**:e0212272.

78. Argentiero A, Muscogiuri G, Rabbat MG *et al.* The Applications of Artificial Intelligence in Cardiovascular Magnetic Resonance-A Comprehensive Review. *J Clin Med* 2022;**11**, DOI: 10.3390/jcm11102866.

79. Vergani V, Lazzeroni D, Peretto G. Bridging the gap between hypertrabeculation phenotype, noncompaction phenotype and left ventricular noncompaction cardiomyopathy. *J Cardiovasc Med (Hagerstown)* 2020;**21**:192–9.

80. Gopalakrishnan V, Menon PG, Madan S. cMRI-BED: A novel informatics framework for cardiac MRI biomarker extraction and discovery applied to pediatric cardiomyopathy classification. *Biomed Eng Online* 2015;**14 Suppl 2**:S7.

81. Bernardino G, Benkarim O, Sanz-de la Garza M *et al.* Handling confounding variables in statistical shape analysis - application to cardiac remodelling. *Med Image Anal* 2020;**65**:101792.

82. Gillies RJ, Kinahan PE, Hricak H. Radiomics: Images Are More than Pictures, They Are Data. *Radiology* 2016;**278**:563–77.

83. Baessler B, Luecke C, Lurz J *et al.* Cardiac MRI and Texture Analysis of Myocardial T1 and T2 Maps in Myocarditis with Acute versus Chronic Symptoms of Heart Failure. *Radiology* 2019;**292**:608–17.

84. Antonopoulos AS, Boutsikou M, Simantiris S *et al.* Machine learning of native T1 mapping radiomics for classification of hypertrophic cardiomyopathy phenotypes. *Scientific Reports 2021 11:1* 2021;**11**:1–11.

85. Pelliccia A, Sharma S, Gati S *et al.* 2020 ESC Guidelines on sports cardiology and exercise in patients with cardiovascular disease. *Eur Heart J* 2021;**42**:17–96.

86. Wolterink JM, Leiner T, de Vos BD *et al.* Automatic coronary artery calcium scoring in cardiac CT angiography using paired convolutional neural networks. *Med Image Anal* 2016;**34**:123–36.

87. Castelletti S, Zorzi A, Ballardini E *et al.* Molecular genetic testing in athletes: Why and when a position statement from the Italian society of sports cardiology. *Int J Cardiol* 2022;**0**, DOI: 10.1016/J.IJCARD.2022.05.071.

88. Castelletti S, Gray B, Basso C *et al.* Indications and utility of cardiac genetic testing in athletes. *Eur J Prev Cardiol* 2022;**29**:1582–91.

89. Limongelli G, Nunziato M, D'Argenio V *et al.* Yield and clinical significance of genetic screening in elite and amateur athletes. *Eur J Prev Cardiol* 2021;**28**:1081–90.

90. Sheikh N, Papadakis M, Wilson M *et al.* Diagnostic Yield of Genetic Testing in Young Athletes With T-Wave Inversion. *Circulation* 2018;**138**:1184–94.

91. Krittanawong C, Johnson KW, Choi E *et al.* Artificial Intelligence and Cardiovascular Genetics. *Life (Basel)* 2022;**12**, DOI: 10.3390/life12020279.

92. Li C, Sun D, Liu J *et al.* A Prediction Model of Essential Hypertension Based on Genetic and Environmental Risk Factors in Northern Han Chinese. *Int J Med Sci* 2019;**16**:793–9.

93. Juhola M, Joutsijoki H, Penttinen K *et al.* Detection of genetic cardiac diseases by Ca(2+) transient profiles using machine learning methods. *Sci Rep* 2018;**8**:9355.

94. Oguz C, Sen SK, Davis AR *et al.* Genotype-driven identification of a molecular network predictive of advanced coronary calcium in ClinSeq® and Framingham Heart Study cohorts. *BMC Syst Biol* 2017;**11**:99.

95. Burghardt TP, Ajtai K. Neural/Bayes network predictor for inheritable cardiac disease pathogenicity and phenotype. *J Mol Cell Cardiol* 2018;**119**:19–27.

96. Anderson L, Sharp GA, Norton RJ *et al.* Home-based versus centre-based cardiac rehabilitation. *Cochrane Database Syst Rev* 2017;**6**:CD007130.

97. Hansen D, Abreu A, Ambrosetti M *et al.* Exercise intensity assessment and prescription in cardiovascular rehabilitation and beyond: why and how: a position statement from the Secondary Prevention and Rehabilitation Section of the European Association of Preventive Cardiology. *Eur J Prev Cardiol* 2022;**29**:230–45.

98. Lamberti V, Palermi S, Franceschin A *et al.* The Effectiveness of Adapted Personalized Motor Activity (AMPA) to Improve Health in Individuals with Mental Disorders and Physical Comorbidities: A Randomized Controlled Trial. *Sports* 2022;**10**, DOI: 10.3390/sports10030030.

99. Compagno S, Palermi S, Pescatore V *et al.* Physical and psychological reconditioning in long COVID syndrome: Results of an out-of-hospital exercise and psychological - based rehabilitation program. *IJC Heart & Vasculature* 2022;**41**:101080.

100. Lee S, Chu Y, Ryu J *et al.* Artificial Intelligence for Detection of Cardiovascular-Related Diseases from Wearable Devices: A Systematic Review and Meta-Analysis. *Yonsei Med J* 2022;**63**:S93–107.

101. Krittanawong C, Rogers AJ, Johnson KW *et al.* Integration of novel monitoring devices with machine learning technology for scalable cardiovascular management. *Nat Rev Cardiol* 2021;**18**:75–91.

102. Nahavandi D, Alizadehsani R, Khosravi A *et al.* Application of artificial intelligence in wearable devices: Opportunities and challenges. *Comput Methods Programs Biomed* 2022;**213**:106541.

103. Inui T, Kohno H, Kawasaki Y *et al.* Use of a Smart Watch for Early Detection of Paroxysmal Atrial Fibrillation: Validation Study. *JMIR Cardio* 2020;**4**:e14857.

104. Prasitlumkum N, Cheungpasitporn W, Chokesuwattanaskul A *et al.* Diagnostic accuracy of smart gadgets/wearable devices in detecting atrial fibrillation: A systematic review and meta-analysis. *Arch Cardiovasc Dis* 2021;**114**:4–16.

105. Belani S, Wahood W, Hardigan P *et al.* Accuracy of Detecting Atrial Fibrillation: A Systematic Review and Meta-Analysis of Wrist-Worn Wearable Technology. *Cureus* 2021;**13**:e20362.

106. Wasserlauf J, Vogel K, Whisler C *et al.* Accuracy of the Apple watch for detection of AF: A multicenter experience. *J Cardiovasc Electrophysiol* 2023, DOI: 10.1111/jce.15892.

107. Ip JE. Wearable Devices for Cardiac Rhythm Diagnosis and Management. *JAMA - Journal of the American Medical Association* 2019;**321**:337–8.

108. Pasadyn SR, Soudan M, Gillinov M *et al.* Accuracy of commercially available heart rate monitors in athletes: a prospective study. *Cardiovasc Diagn Ther* 2019;**9**:379–85.

109. Strik M, Caillol T, Ramirez FD *et al.* Validating QT-Interval Measurement Using the Apple Watch ECG to Enable Remote Monitoring During the COVID-19 Pandemic. *Circulation* 2020;**142**:416–8.

110. Castelletti S, Dagradi F, Goulene K *et al.* A wearable remote monitoring system for the identification of subjects with a prolonged QT interval or at risk for drug-induced long QT syndrome. *Int J Cardiol* 2018;**266**:89–94.

111. Chowdhury MEH, Alzoubi K, Khandakar A *et al.* Wearable Real-Time Heart Attack Detection and Warning System to Reduce Road Accidents. *Sensors (Basel)* 2019;**19**, DOI: 10.3390/s19122780.

112. Orchard JJ, Orchard JW, Raju H *et al.* Comparison between a 6-lead smartphone ECG and 12-lead ECG in athletes. *J Electrocardiol* 2021;**66**:95–7.

113. Peritz DC, Howard A, Ciocca M *et al.* Smartphone ECG aids real time diagnosis of palpitations in the competitive college athlete. *J Electrocardiol* 2015;**48**:896–9.

114. Caamal-Herrera A;, Atoche-Enseñat K;, Estrada-López R; *et al.* Energy Efficient Framework for a AIoT Cardiac Arrhythmia Detection System Wearable during Sport. *Applied Sciences 2022, Vol 12, Page 2716* 2022;**12**:2716.

115. Green EM, van Mourik R, Wolfus C *et al.* Machine learning detection of obstructive hypertrophic cardiomyopathy using a wearable biosensor. *NPJ Digit Med* 2019;**2**:57.

116. Seshadri DR, Thom ML, Harlow ER *et al.* Wearable Technology and Analytics as a Complementary Toolkit to Optimize Workload and to Reduce Injury Burden. *Front Sports Act Living* 2021;**2**:1–17.

117. Yildiz O, Stano K, Faraji S *et al.* High performance carbon nanotube – polymer nanofiber hybrid fabrics. *Nanoscale* 2015;**7**:16744–54.

118. Bayoumy K, Gaber M, Elshafeey A *et al.* Smart wearable devices in cardiovascular care: where we are and how to move forward. *Nat Rev Cardiol* 2021;**18**:581–99.

119. Fanous Y, Dorian P. Wearables for cardiac monitoring in athletes: precious metal or fool's gold? *European Heart Journal - Digital Health* 2021;**2**:358–60.

120. Gerke S, Minssen T, Cohen G. Ethical and legal challenges of artificial intelligence-driven healthcare. *Artificial Intelligence in Healthcare* 2020:295–336.

121. Leslie D. Understanding artificial intelligence ethics and safety. (arXiv:1906.05684v1 [cs.CY]). *arXiv Computer Science*.

122. Lisboa PJG, Jayabalan M, Ortega-Martorell S *et al.* Enhanced survival prediction using explainable artificial intelligence in heart transplantation. *Sci Rep* 2022;**12**:19525.

123. Walters B, Ortega-Martorell S, Olier I *et al.* How to Open a Black Box Classifier for Tabular Data. *Algorithms* 2023;**16**, DOI: 10.3390/a16040181.

124. Gunning D, Stefik M, Choi J *et al.* XAI-Explainable artificial intelligence. *Sci Robot* 2019;**4**, DOI: 10.1126/scirobotics.aay7120.

125. Briganti G, Le Moine O. Artificial Intelligence in Medicine: Today and Tomorrow. *Front Med (Lausanne)* 2020;**7**:27.

126. Huang KC, Lin CE, Lin LY *et al.* Data-driven clustering supports adaptive remodeling of athlete's hearts: An echocardiographic study from the Taipei Summer Universiade. *Journal of the Formosan Medical Association* 2022;**121**:1495–505.

127. Bernardino G, Benkarim O, Sanz-de la Garza M *et al.* Handling confounding variables in statistical shape analysis - application to cardiac remodelling. *Med Image Anal* 2020;**65**, DOI: 10.1016/J.MEDIA.2020.101792.

128. Viviers PL, Kirby JAH, Viljoen JT *et al.* The Diagnostic Utility of Computer-Assisted Auscultation for the Early Detection of Cardiac Murmurs of Structural Origin in the Periodic Health Evaluation. *Sports Health* 2017;**9**:341–5.

129. Narula S, Shameer K, Salem Omar AM *et al.* Machine-Learning Algorithms to Automate Morphological and Functional Assessments in 2D Echocardiography. *J Am Coll Cardiol* 2016;**68**:2287–95.

130. Whiting PF, Weswood ME, Rutjes AWS *et al.* Evaluation of QUADAS, a tool for the quality assessment of diagnostic accuracy studies. *BMC Med Res Methodol* 2006;**6**, DOI: 10.1186/1471-2288-6-9.

131. Adetiba E, Iweanya VC, Popoola SI *et al.* Automated detection of heart defects in athletes based on electrocardiography and artificial neural network. *Cogent Eng* 2017;**4**, DOI: 10.1080/23311916.2017.1411220.

132. Castillo-Atoche A, Caamal-Herrera K, Atoche-Enseñat R *et al.* Energy Efficient Framework for a AIoT Cardiac Arrhythmia Detection System Wearable during Sport. *Applied Sciences (Switzerland)* 2022;**12**, DOI: 10.3390/APP12052716.

133. Barbieri D, Chawla N, Zaccagni L *et al.* Predicting cardiovascular risk in athletes: Resampling improves classification performance. *Int J Environ Res Public Health* 2020;**17**:1–9.

134. Bellazzi R, Zupan B. Predictive data mining in clinical medicine: current issues and guidelines. *Int J Med Inform* 2008;**77**:81–97.