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Artificial Intelligence models in autoimmune disease prediction: Current applications, challenges, and future perspectives

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Abstract

Autoimmune diseases are heterogeneous immune-mediated disorders characterized by loss of immunological tolerance, autoantibody production, variable clinical manifestations, and unpredictable disease progression. These features make early diagnosis, risk stratification, and treatment-response prediction challenging using conventional clinical assessment alone. Artificial intelligence has emerged as a promising approach for improving autoimmune disease prediction through the analysis of complex and multidimensional healthcare data. This narrative review summarizes current applications of artificial intelligence models in autoimmune disease prediction, with emphasis on machine learning, deep learning, natural language processing, computer-aided diagnosis, and predictive modeling. Relevant literature was reviewed to describe major AI models, data sources, disease-specific applications, image-based diagnostic systems, challenges, and future perspectives. AI-based prediction in autoimmune diseases commonly uses clinical data, electronic health records, genomic and proteomic profiles, imaging data, and wearable-device outputs. These approaches have been applied in rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, type 1 diabetes, autoimmune liver diseases, Sjögren's syndrome, and celiac disease to support diagnosis, patient stratification, disease monitoring, treatment-response prediction, and personalized management. However, clinical implementation remains limited by small datasets, disease heterogeneity, lack of external validation, privacy concerns, interpretability issues, and integration barriers. Overall, artificial intelligence may strengthen precision medicine in autoimmune diseases, but its routine clinical use requires validated, explainable, and ethically implemented models supported by multidisciplinary collaboration.

Keywords: Artificial Intelligence; Autoimmune Diseases; Predictive Modeling; Precision Medicine; Computer-Aided Diagnosis

1. Introduction

Autoimmune diseases (AIDs) develop when immunological tolerance is disrupted, allowing autoreactive immune cells to recognize self-molecules as foreign targets and stimulate the production of autoantibodies. There is a wide range of pathogeneses of AIDs, which include both hereditary predisposition and environmental aspects. Non-genetic risk factors have been proved by the absence of perfect agreement in autoimmunity between monozygotic twins and differences in the prevalence of autoimmune diseases among different populations. Between 3 to 5% of all individuals are affected by AIDs, and it is also possible for more than one type of disease to be developed by an individual, hence having similar pathogeneses. Although AIDs are not considered major life-threatening conditions, they make people disabled [1,2].

The most common forms of autoimmune disorders associated with rheumatic disease include Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), Sjogren's Syndrome (SS), Inflammatory Myopathies (IM), and Systemic Sclerosis (SSc). These conditions are characterized by significant heterogeneity in terms of clinical

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manifestations as well as biological aspects. This variability poses challenges in treatment, particularly when it comes to the implementation of biological DMARDS. Therefore, new strategies should be developed to enhance prediction of drug response in the context of precision medicine [3].

From the perspective of the health care system, the cost increase, demands from the general population, and policy pressure in providing coordinated care across many health care institutions requires that there should be a method that will ensure the integration of healthcare information within different sections. It is due to advancements in AI technology that it has become possible to create models based on integrated healthcare information that would predict disease occurrence [4].

AI methods, including ML and DL, have become more popular in digital healthcare tools used to facilitate disease prediction and diagnoses, and the analyses of biomedical data sets. The ML methods are able to handle vast and intricate data sets, identify key features within the data sets, and perform effective classification of the data, particularly those associated with medical images and signals [5].

Therefore, the main goal of conducting this review was to provide a brief description of the current applications of AI models in predicting autoimmune diseases based on the approaches used, the types of data used to train them, fields of predictions in terms of various autoimmune disorders, and the limitations associated with using AI for this purpose.

2. Search Strategy and Selection Criteria

The main purpose of this narrative review is to present a summary of evidence concerning the use of artificial intelligence models for predicting autoimmune diseases, taking into account machine learning, deep learning, computer-aided diagnosis and predictions, and precision medicine. The chosen articles are linked with the mechanisms of autoimmune diseases, their classification, artificial intelligence models in healthcare, predictions through artificial intelligence, modeling, the source of data for developing models, application of artificial intelligence in various diseases, CAD systems based on images, and also challenges to the use of such technologies. The articles chosen are those that have been published since 2021 with only a few exceptions concerning the basic definitions in the field. Selection criteria involved works which have covered topics such as AI, machine learning, deep learning, NLP, CAD, EHR-based prediction, genomic/predictive analytics prediction, imaging, wearable device-based monitoring, or treatment response prediction, in the area of autoimmune diseases. The exclusion criteria involved the following features: (1) being irrelevant to the prediction of autoimmune diseases; (2) lack of involvement of AI for any research purposes; (3) covering areas other than medical applications using AI; and (4) lacking contributions towards diagnosis, prediction, monitoring, stratification, and personalized treatment.

3. Overview of autoimmune diseases

The continuation of the autoimmune response is possible through the process of the autoimmune cycle that includes the presentation of autoantigens which have been released from damaged tissues through the help of dendritic cells in the local lymph nodes. At the lymph nodes, the autoantigens get processed and then presented to naïve T-cells and B-cells using co-stimulation such as B7-CD28. As a result of activation, the helper T cells cause induction of effector immune response through cytokines while the activated B cells have the ability to develop into plasma cells that secrete autoantibodies. The immune responses created consequently travel back to the areas where there are damages caused by the autoantigenic tissues leading to more damages, hence releasing more autoantigens that start another immune response [2,6].

Indeed, despite having intact immune mechanisms, only a very small number of autoreactive T and B cells can escape from the tolerance mechanisms that take place in both the central and peripheral levels. However, under normal circumstances, the autoreactive T and B cells will not cause any harm until a genetically predisposed individual comes across certain environmental factors that induce the loss of tolerance. The damage to the tissues causes the liberation of the autoantigen into the tissues where it is carried to secondary lymphoid organs through lymphatics or by the antigen-presenting cells found in tissues. These effector cells are released from the lymphoid compartments and migrate back to those areas that are rich in antigens, hence increasing tissue damage [2].

The progression of autoimmune disease could occur via three different stages; these stages include initiation, propagation, and resolution. The initiation phase refers to the breaking of the immune system's tolerance brought about by both genetic and environmental triggers before symptoms arise. The propagation phase entails the induction of inflammatory responses, which include cell/tissue injury and exposure to autoantigens, resulting in epitope spreading and additional immunogenic targets. Regulatory cells and cytokines play important functions in establishing a feedback mechanism within inflammation. Resolution includes regulatory processes whereby T-regulatory cells function under the control of certain genes such as FOXP3. Deficiencies in regulatory mechanisms, for example, FOXP3, CTLA-4, PD-1, B-regulatory cells, CD22, FcγRIIB, or PD-L1, may trigger autoimmune diseases [7,8].

There exist many mechanisms by which autoimmune injuries to body organs occur. These may involve the stimulation of autoantibodies that cause receptor activity as seen in Graves' disease; blockade of autoantibodies that block the receptors from functioning as is the case in myasthenia gravis; deposition of immune complexes and their activation to bring about inflammation and injury to organs, for instance in glomerulonephritis; and also innate immune receptors such as Toll-like receptors attacking self-antigens. Pathogens such as EBV, CMV, *H. pylori*, rubella virus, and coronavirus SARS-COV-2 may induce an autoimmune reaction through mechanisms like molecular mimicry, neoantigen formation, tissue damage, and the formation of autoantibodies. Additionally, both COVID-19 infection and, in very rare cases, vaccination for COVID-19 have been described as potential causes [7,9].

4. Artificial intelligence in healthcare

Artificial intelligence (AI) has become an important approach in healthcare because it can analyze large and complex clinical datasets and extract useful patterns that support medical decision-making. This kind of technology might assist physicians to diagnose a patient's illness, develop a treatment plan, estimate the risks involved, and provide a prognosis about the condition. Applications of this form of AI require healthcare data that is created during activities such as screening, diagnosis, lab tests, imaging, genotyping, and documentation [10,11].

Examples of artificial intelligence approaches that have been applied in healthcare include machine learning, deep learning, and natural language processing. Machine learning is employed to process structured data such as imaging, genomics, electrophysiology, and laboratory reports while natural language processing transforms unstructured data in texts to machine-readable formats. Some examples of machine learning approaches are supervised, unsupervised, and semi-supervised learning. These involve support vector machines and neural networks [10,12–14].

Deep learning represents a complex neural network model and works best for data with many dimensions in medicine, particularly imaging. Convolutional neural networks have been shown to be very efficient in detecting problems through imaging in cases like congenital cataracts, skin cancer, and diabetic retinopathy [15–17]. Application of AI in clinical practice is currently limited to cancers, neurologic conditions, and cardiovascular diseases. An example of AI application has been stated with reference to stroke with regard to its role in early detection and diagnosis, treatment decision making, and prognostication. The application of AI in clinical practice requires further validation, regulation, and standardization [10].

5. AI models used in autoimmune disease prediction

Some of the most widely used artificial intelligence approaches to predict autoimmune diseases include the machine learning approaches as they are capable of analyzing different types of data such as clinical data, laboratory data, genetic data, image-based data, and omics data. Machine learning models have been applied in the case of autoimmune diseases to support diagnosis, identify patient sub-types, identify organs targeted by the disease, evaluate disease progression, and treatment response prediction. Recent reviews indicate that machine learning approaches can be helpful in developing diagnostic algorithms for autoimmune diseases [18].

A supervised learning model would be quite relevant when making predictions about an autoimmune disease because such models depend on the patient's disease outcome that will help create an algorithm to categorize or make predictions. Some of the examples of these types of models include the logistic regression model, the support vector machine model, the random forest model, the gradient boosting model, and the neural network model. This type of model is especially useful when there is more than one variable in autoimmune disease prediction because autoimmune diseases have various types of categorization [18,19].

In relation to systemic lupus erythematosus, there is research using machine learning approaches for developing an automated diagnosis support system for the disease, known as the Systemic Lupus Erythematosus Risk Probability Index (SLERPI). SLERPI is intended to be developed as a machine learning-based system for aiding diagnosis and offering risk probability scores based on both clinical and immunological factors [20].

Development of predictive models for determining drug responses in patients having rheumatoid arthritis was accomplished using the technique of developing predictive models that employed machine learning algorithms. Techniques like random forest, XGBoost, artificial neural network algorithm, support vector machines, and others have been used extensively in research involving patients having RA in order to determine the predictors of resistance or responsiveness to biological disease-modifying anti-rheumatic drugs. It would seem that tree-based machine learning algorithms like random forest and gradient boosting would be effective [21–23].

The deep learning models have mainly been used when the prediction of autoimmune diseases depends on image information. This includes such cases as cutaneous lupus erythematosus, which utilized a smart phone application that employed deep learning models for classification. This shows the capabilities of image-based AI techniques in detecting complicated autoimmune conditions in the skin. This is relevant to predicting autoimmune diseases due to the fact that there are autoimmune diseases of the skin that depend on image analysis [24].

In addition, AI techniques have also found use in object detection algorithms and convolutional neural networks. The use of deep learning algorithms has been seen in cases of Sjogren's syndrome to detect images from salivary gland biopsy for diagnosis of lymphocyte infiltration. From this example, we can see that prediction through AI techniques in the field of auto-immune diseases is not limited to clinical data, but also involves pathology data [25,26].

With regard to autoimmune diseases of the liver and rheumatology, there is increasing application of AI models for purposes other than diagnosis and more specifically as a tool for practicing precision medicine. Data collected clinically, through imaging, lab tests, and at the molecular level may be incorporated into AI systems to assist in risk stratification, prognostication, monitoring, and predicting treatment responses. On the other hand, several reviews in literature have pointed out the continued presence of limitations associated with data size, heterogeneous phenotypes, non-validation, interpretability, and inadequate clinical translation [3,27,28].

6. Data sources for AI-based prediction

Table 1 presents the main sources of information that are used for generating predictions based on AI in autoimmune diseases. Direct information about patients' conditions is provided by clinical and electronic health records. Genomics and proteomics are useful in detecting risk factors and identifying biomarkers. Image analysis is appropriate for deep learning purposes related to the evaluation of tissues/organs. Wearable sensors can be applied for the continuous monitoring of patients with autoimmune diseases characterized by episodes of exacerbation.

Table 1 Data sources for AI-based prediction in autoimmune diseases

Data source	**Main information included**	**Role in AI-based prediction**	**Relevance to autoimmune diseases**	**Key references**
Clinical data	Demographic features, symptoms, disease duration, clinical scores, laboratory findings, treatment history, and outcome measures	Used by machine learning models to support diagnosis, patient stratification, disease-progression prediction, and treatment-response estimation	Particularly useful in autoimmune rheumatic diseases because patients show high clinical heterogeneity and variable therapeutic responses	[3,18]
Electronic health records (EHRs)	Diagnoses, laboratory results, medication history, clinical encounters, recorded symptoms, and longitudinal patient information	Used to detect patients who may require autoimmune disease evaluation before formal diagnosis	Can support earlier recognition of systemic autoimmune rheumatic disease patterns and guide referral or autoantibody testing decisions	[29]
Genomic data	Genetic variants, single nucleotide polymorphisms, genome-wide association data, and polygenic risk scores	Incorporated into AI models to improve disease-risk estimation, classification, and early diagnostic prediction	Relevant because autoimmune diseases often have a genetic susceptibility component; used in SLE and RA prediction models	[30–32]

Proteomic data	Circulating proteins, biological pathway markers, and disease-related protein signatures	Integrated with clinical and omics data to identify candidate biomarkers and classify patients by disease stage or treatment response	May reflect autoimmune activity, disease subtype, disease onset, and therapeutic response, especially in rheumatoid arthritis	[33,34]
Imaging data	Radiological images, histopathological images, organ-specific structural changes, and digital pathology features	Used mainly by deep learning models, especially convolutional neural networks, for automated feature extraction and image-based classification	Useful in autoimmune diseases with tissue, organ, or biopsy-based diagnostic features, such as Sjögren's syndrome and autoimmune liver diseases	[26,27]
Wearable devices	Physical activity, mobility, heart rate, sleep-related data, fatigue-related indicators, and symptom-related digital signals	Provides patient-generated data for continuous monitoring and prediction of disease activity outside clinical settings	Particularly relevant for autoimmune diseases with fluctuating activity, intermittent flares, and need for remote monitoring	[35]

7. Common AI models used in autoimmune disease prediction.

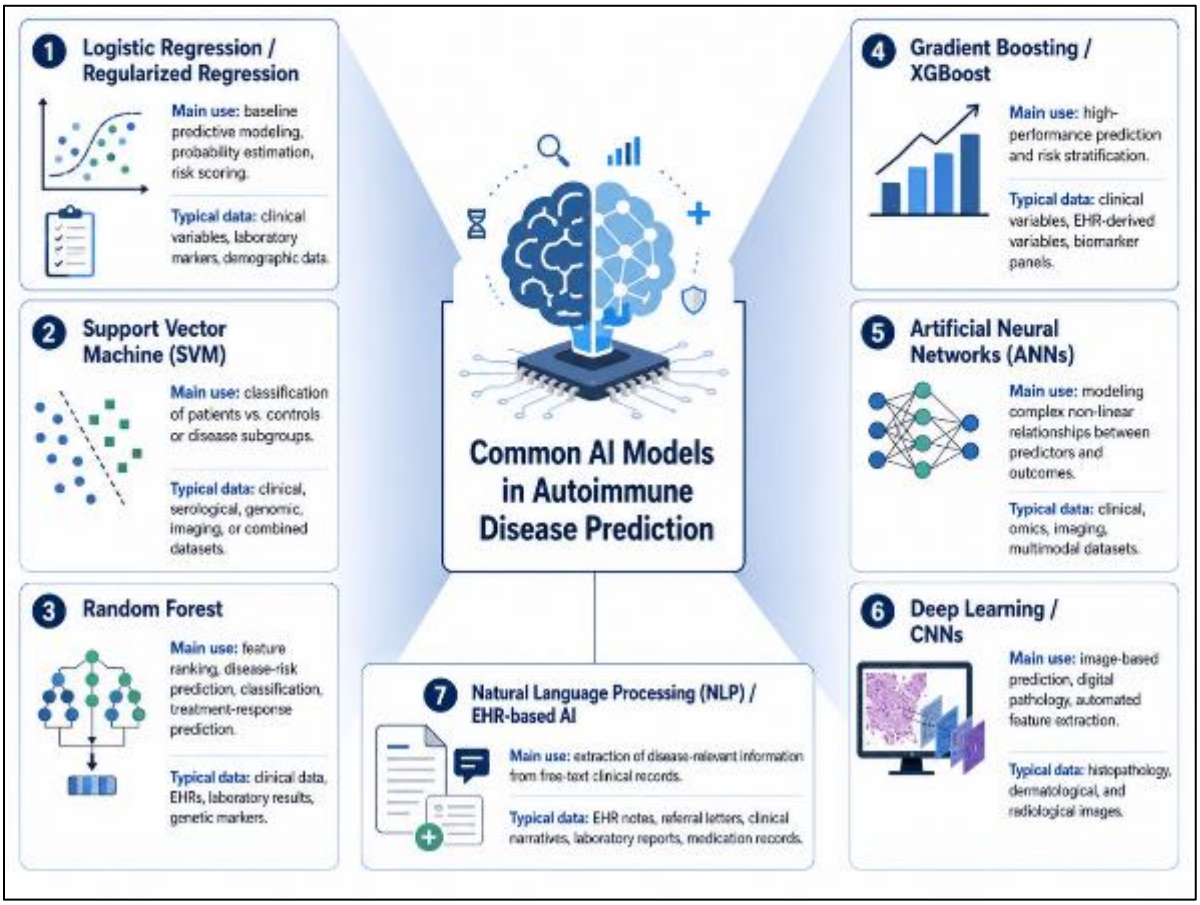

Figure 1 Common AI models used in autoimmune disease prediction (Figure was designed using ChatGPT based on information extracted from references [3,18,20,22,23,26,27,29]).

Examples of commonly used AI models to predict autoimmune disease include traditional statistical models, supervised machine learning models, neural network modeling techniques, deep learning, and NLP models. Traditional models are ideal for risk assessment using interpretation. Examples of supervised machine learning models that work well in structured data, like clinical, lab, and genetic data, include random forest, support vector machines (SVM), and gradient boosting models. Convolutional neural networks (CNN) work best with images from histopathology and dermatology (Figure 1).

8. Applications of AI for specific autoimmune diseases

Application of Artificial Intelligence technology was mainly oriented towards diagnostics, activity state evaluation, disease course prediction and outcome and therapeutic efficiency in RA patients. The fact of great variability between RA patients makes it possible to apply the technology of machine learning for classification and prediction of therapy response, including biological DMARDs. Several modern reviews state that application of machine learning could be helpful in identification of patients responding and non-responding to therapy before starting of biological DMARDs, and thus making it possible to adopt a precision medicine strategy in RA patients [3,19].

Many reasons may exist to utilize artificial intelligence in the field of SLE as it presents heterogeneity in terms of clinical presentations and autoantibody presentations. Some machine learning models have been developed to assist with diagnosing SLE, as well as identifying those patients who need a further evaluation from a rheumatology or autoimmune perspective. For example, the SLE Risk Probability Index has been devised to facilitate the diagnosis of SLE with the help of both clinical and immunological criteria [20]. Moreover, the use of EHR machine learning algorithms for predicting which patients need autoimmune disease workup before their diagnosis has been found to be very useful in systemic autoimmune rheumatic diseases [29].

The application of artificial intelligence in multiple sclerosis (MS) can be noted through the imaging-based diagnosis of MS, lesion recognition, monitoring the course of the disease, and its prediction of progression. AI algorithms and deep learning methods are helpful in classifying MS cases using features obtained from MRI scans together with other clinical data. As per a systematic literature review of 103 studies, artificial intelligence technology, machine learning algorithms, and statistical methods have gained much attention for diagnosing multiple sclerosis, despite some limitations related to clinical data access [36].

The use of AI-based predictions in terms of type 1 diabetes (T1D) refers to the utilization of algorithms for identifying patients who are likely to be affected by the disease. These algorithms may take into account data such as antibodies, genetics, metabolism, clinical parameters, as well as monitoring data to improve the precision of prediction. According to the findings of a recent systematic review, several types of machine learning algorithms including logistic regression, support vector machines, random forests, and artificial neural networks have been used in diagnosing T1D [37].

Regarding autoimmune diseases of the liver, the use of artificial intelligence technology in these diseases has been proposed as a way towards precision medicine concerning the disease's diagnosis, prognosis, risk stratification, and assessment of the response to treatment. Such diseases generate diverse kinds of data that can be used in applying the AI techniques to analyze the data in a multimodal manner. Artificial intelligence can help meet several unmet challenges regarding autoimmune liver diseases, including patient stratification, biomarker identification, and non-invasive monitoring of patients [27].

However, when dealing with celiac disease, there have been instances where AI technologies were used to aid in making diagnoses based on the use of clinical, serologic, genetic, and histopathologic data. It is possible that artificial intelligence-based diagnostic tools can be employed to diagnose people who are at risk of contracting the disease as well as analyze biopsies of the duodenum. In recent times, there were attempts to employ machine learning techniques to predict patients who will develop autoimmune celiac disease before making an initial diagnosis of the condition [38,39].

9. Computer-aided diagnosis and image-based AI

Computer-aided diagnosis/detection (CAD) represents an application that seeks to assist medical professionals in interpreting medical images [40]. It is important to note that the same CAD application has been described using different terminologies including medical expert systems, computer-assisted medical diagnosis, and computerized diagnostic evaluation [41]. The significance of CAD cannot be overstated in light of the fact that the radiologists and pathologists must interpret voluminous imaging information that has been obtained using radiography, x-ray, MRI, CT, and ultrasound scans. This is accomplished through the application of computer vision in recognizing certain patterns in digital pictures or video images. The approach makes use of concepts from artificial intelligence, computer vision, pathology, and image processing of radiologic images. Even though CAD technology has been in use for quite some time in clinical practice, its use has been supplementary rather than primary [42].

Developing a CAD system always involves a number of key AI technologies. To begin with, there is data gathering, which requires the availability of high-quality medical data for the development of diagnostic models. However, the absence of access to diverse images within the medical database is the major obstacle in the development of CAD systems. Then comes the phase of data pre-processing, which is aimed at improving the quality of data by eliminating noise and labeling the data in order to use them for model training. Finally, image segmentation is performed. Lastly, the detection process involves identifying areas of interest that are considered abnormal within medical images, including tumors, lesions, nodules, or any other abnormalities. The final steps involve classification and performance evaluation of images/cases using learning techniques both supervised and unsupervised to classify and evaluate their accuracy in diagnosing CAD systems [42–44] (Figure 2).

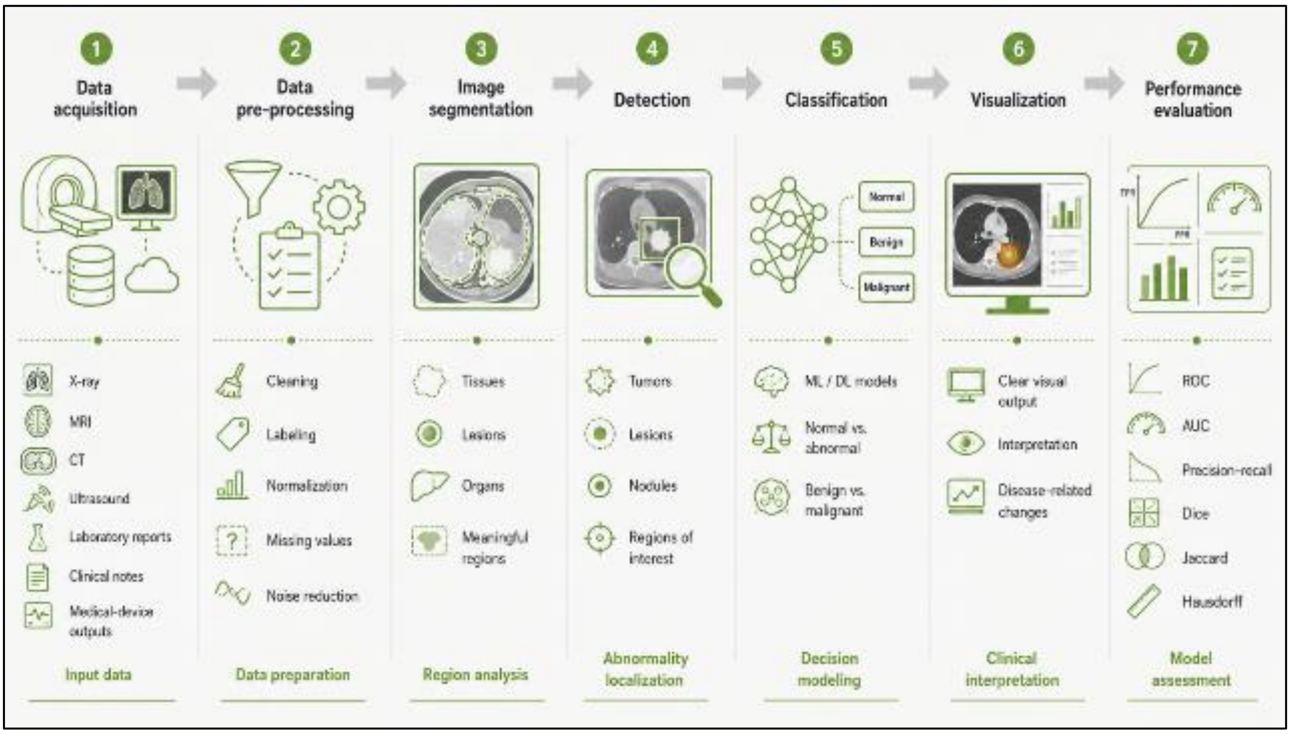

Figure 2 Main steps of CAD and image-based AI for medical diagnosis (Figure was designed using ChatGPT based on information extracted from [42])

10. Predictive modeling and personalized medicine

As far as personalized medicine is concerned, the application of predictive modeling will play an essential role in converting heterogeneous patient data into personalized risk estimates. In auto-immune diseases, the concept of personalized medicine will play an essential role because every individual case presents differently in terms of how the illness manifests itself, the immune system's traits, the body part affected, and the efficacy of the therapy used. By leveraging the power of artificial intelligence in predictive models, one can make use of different types of data including clinical, laboratory, and imaging test results, and electronic medical record information [4].

In auto-immune rheumatology, the use of predictive modeling is more focused on predicting responses to drugs and individualized treatment. Recently, studies have shown that there are some cases where AI technology can be applied for diagnoses, risk stratification, prediction of the prognosis, and drug response in auto-immune rheumatic diseases. The reason why such prediction would prove helpful is because these diseases can vary from one person to another, meaning their drug response would differ accordingly [3].

Thus, the EHR system will serve as a foundation for making predictions before the diagnosis of any autoimmune disease. According to research carried out by Forrest et al., a machine learning algorithm was built to identify which patients required a rheumatology visit for their systemic autoimmune rheumatic diseases using long-term electronic health records of 161,584 individuals [29]. Hence, predictions in cases of autoimmune diseases can be made using the data gathered from EHRs.

The employment of remote sensing technology and multi-modal predictive systems can be additional techniques that help personalize medicine. In the case of digital health solutions and machine learning, their use has been demonstrated in rheumatoid arthritis, in which patient reports were used together with digital indicators collected through everyday activities for remote analysis of the illness's state and its impacts. It may seem realistic that the mentioned methods will help complement traditional clinical assessments, especially when dealing with an illness whose symptoms are highly variable and consist of episodes of flare-ups. Yet, several important factors should be considered for their future implementation in clinics [4,35].

Challenges and limitations

Although the application of AI models for the risk prediction in autoimmunity is growing, there are still various obstacles that prevent their application. The differences among autoimmune diseases in terms of their manifestations, biology, evolution, and response to treatment create difficulties in designing such models. Most AI models have been developed using a small number of patients under specific disease conditions or even within one institution. Their performance might be influenced by the fact that they will be applied in another setting. Furthermore, various datasets should be appropriately processed and labeled. The ability to explain and understand also becomes critical here, mainly because of the need to have an understanding of what affects the prediction of risks by the system in order for doctors to use the results for management purposes. Therefore, some of the main concerns include external validation, data heterogeneity, privacy, explainability, regulation, and integration into practice.

Future perspectives

In order for prediction via AI technology for autoimmune diseases to move into the future, it is essential for it to move away from mere prediction and focus more on validation and integration of various modalities such as clinical data, EHRs, genomic and proteomic data, imaging, and patient-generated data from wearables. This will allow for early detection, risk stratification, monitoring, and treatment prediction for fluctuating levels of autoimmune disorders. Modeling from EHRs is expected to play an important role in identifying those patients who need to go through autoimmune screening or consult with a rheumatologist. Also, the usage of wearable sensors is expected to be helpful in remote monitoring of flare-ups and activity. Also, federated learning can be used in order to train models from various healthcare databases simultaneously while ensuring that privacy remains intact, and explainability can be leveraged by physicians for understanding how AI makes some predictions.

11. Conclusion

Utilization of AI technology has brought immense opportunities for the improvement of autoimmune disease prediction by combining various types of data sets through methodologies like machine learning, deep learning, natural language processing, and computer-aided diagnosis. Some of the latest developments indicate that AI algorithms could be employed in helping predict early diagnosis, patient stratification, disease activity, treatment response, and image diagnosis among other applications of autoimmune disorders including rheumatoid arthritis, systemic lupus erythematosus, multiple sclerosis, type 1 diabetes, autoimmune liver disease, Sjogren's syndrome, and celiac disease. However, at present, they should be viewed as supplements to decision making and not as substitutes. Their successful implementation will depend upon having bigger databases, being independently validated, ethical use, and effective incorporation into health care systems. In summary, although AI technology has a lot of potential for helping precision medicine in autoimmune diseases, its clinical implementation is difficult.

Compliance with ethical standards

Disclosure of conflict of interest

The author declares no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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