ARTIFICIAL INTELLIGENCE THEORY and APPLICATIONS

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Artificial Intelligence Applications in Hematology

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A B S T R A C T

Artificial intelligence (AI) is a computer-based science that aims to simulate the human brain using a system. One of the most used areas of artificial intelligence in medicine is hematology. In this study, the Pubmed database was scanned using the words "hematology, artificial intelligence". The chronological development of artificial intelligence in hematology was evaluated by examining the articles found. AI was used firstly in hematology with peripheral blood interpretation in laboratory systems. It was followed by flow cytometry for immunophenotyping and bone marrow reporting. The diagnosis of iron deficiency anemia, hemoglobinopathies, Polistemia Vera and classification of hematological malignancies such as leukemia and lymphoma were made. AI-supported algorithms are developed for immunotherapy and evaluation of recipient compatibility before stem cell transplantation. Also they used evaluation of recurrence and complications after transplantation. Together with the new generation digital image analyzers, images has been transferred to a central laboratory and an unique automation that can be archived with fast, high-quality consultation. As a result, artificial intelligence systems have been used in the diagnosis and treatment of hematological diseases from past to present and seem to play an important role in the future.

1. Introduction

Today, "Medical artificial intelligence" programs have been used in medicine increasingly. Artificial intelligence (AI) systems can also make clinical diagnosis and treatment recommendations based on patient data and advise the physician. Artificial neural networks are mimic the work of the biological nervous system. They are detecting patterns that have not been noticed before and classing them, checking medical devices, detecting the characteristics of medical images. Hematology is the area where medical AI is mostly used. AI is used in benign and malignant hematology for diagnosis, prognosis, treatment planning as well as hematologic pathological, radiographic, laboratory, genomics, pharmacological and chemical data related. In this study, Pub med database was scanned using the words

"hematology, artificial intelligence". The chronological development of artificial intelligence was evaluated in hematology from the past to date by examining the found articles.

2. History

In 1873, Alexander Bain (1818–1913) described memory as a series of nerves and published the book "Relationships of mind and body theories" [1]. In 1943, Warren S. McCulloch, a neuroscientist, and Walter Pitts, a logician, made a mathematical model of a neuron. They wrote an article titled "The logical calculus of ideas implicit in neural activity" [2]. In 1950, Alan M. Turing, one of the fathers of modern computer science, proposed a criterion called the "Turing test" to decide whether a computer program achieves an intelligence equivalent to human. In this test, a person has a written conversation with a reporter who does not appear on any subject. If a person believes that he is talking to another person while communicating with a computer, the computer passes the Turing test. At John McCarthy's conference in 1956, the term AI was officially added to the dictionary of scientific terms. In 1960, Rosenblatt presented the first learning machine capable of learning to identify optical patterns, developing the first neural network to be applied to a real problem [3].

3. Artificial intelligence and hematology

AI first applications in hematology are related to laboratory diagnosis. In 1995, a three-legged system was established in five European hospitals aimed at accurate diagnosis and classification of hematological malignancies by conducting diagnostic peripheral blood interpretation, flow cytometry immune phenol typing and bone marrow reporting. These systems are named after their creators as Professor Petrushka, Fidelio and Belmonte respectively. In addition to laboratory results, these three modules are engaged in interaction with each other and with a database that includes clinical history. With this system, the diagnosis and classification of 100 definitively diagnosed leukemia patients were made. While the system correctly diagnosed 94 patients, the correct diagnosis level of the clinicians was determined as 99[4]. Then 366 samples of patients with lymphoproliferative disorders, leukemias and lymphomas collected from two independent medical centers tested for control. In 300/366 samples, a common result was achieved with Fidelio's interpretations. When analyzing the disputes, it revealed that most of them were due to errors in the diagnostic record and differences in diagnostic criteria between Fidelio's database of information and those used in the medical center [5]. Bone marrow reporting by the Professor Belmonte system; 785 random cases were evaluated and scored by three hematologists: one consultant, one senior and one teenager. Each of the reports scored satisfactory or better than at least two of the three referees. In addition to safety and accurateness, improving efficiency by reducing turnaround time has also been found to be an important feature of the system [6].

Another approach to the diagnosis of hematological diseases was achieved through unsupervised pattern recognition and the integration of artificial neural networks (ANN). In 1999, Fucharoen worked on an artificial intelligence laser cytometer device that was adapted to the ADVIA120 automatic hematological analyzer. It has classed 40,000 red blood cells of this device by volume and Hb content to base it on Mie sweat. In the diagnosis of thalassemia, iron deficiency anemia, hemoglobinopathy patients, relatively accurate results were obtained according to the conditions of that day [7]. In 1995, Erler et al. and Birndorf et al. used artificial intelligence devices in the thalassemia class [8, 9]. Amendolia et al. used four peripheral blood hematological parameters (RBC, Hb, Hct and MCV). They detected beta carrier and alpha carrier thalassemia with 94% accuracy using ANN together with hemochrocytometric analysis [10]. After the development of automatic cytochemistry for leukocyte counting, a new and effective pre-microscopic approach devoloped during automatic blood cell counting for leukemia diagnosis and classification. A cytometer was used that based on the light assessment of basic cell properties, volume, peroxide activity and nuclear density. This device distinguished leukocyte classes according to volume, myeloperoxidase content and chromatin model. Information was learned by adding a score to the cytogram about normal samples as well as the genealogy, myeloid differentiation level and chromatin pattern. Compared to FAB qualification, this system had 91% diagnostic activity [11]. In 2001, this

software was developed. It found normal and pathological differentiation from blood samples taken from patients with hematopoietic disorders [12]. In 2002, using artificial intelligence 98% diagnosis of Polistemia Vera (PV) was possible [13].

In 1999, Golub et al. created a systematic approach to identify acute leukemia. It is based on the simultaneous expression of thousands of genes using independent DNA microdysis[14]. Using genome microdyzis to leukemia classification, it was possible to identify known prognostic leukemia subtypes and special gene signatures of high relapse risk patients. These studies could also be used for studies created to differentiate stem cells into cells that can be used to replace tissue damaged by disease or trauma [15].

AI was also used in the diagnosis of iron deficiency anemia [16]. Neural network-based models have been developed for the differentiative diagnosis of iron deficiency anemia and β-thalassemia [17-21].

Morita et al. analyzed bone marrow samples from patients with myeloid leukemia. They created an AI-based model that accurately predicts clinical phenotype based on somatic mutation data [22]. Siddiqui proposed an AI model based on known clinical parameters before treatment, estimating mortality rates for patients undergoing chemotherapy. Thus, clinicians were allowed to identify patients suitable for intensive induction regimens [23]. These approaches are based on cytogenetics, mutation status, and age. They have been shown to accurately predict the prognosis of acute myeloid leukemia (AML). Gerstung et al. has individually applied large data set knowledge banks to combine clinical and genomic data of patients. This method provided a higher level of accuracy for recurring, remission compared to current standards [24]. Fleming, Shrev, Li et al. reported a lower error rate compared to the European Leukemia Net 2017 score in predicting the prognosis [25-27]. AI can be used to develop a new prognostic index or improve an existing one. Patkar and Wagner developed a scoring system for classification NPM1 mutated AML [28, 29]. AI was able to estimate the probability of a full response in pediatric AML patients receiving induction therapy according to gene expression models [30]. AI can provide a patient selection of new therapeutic agents approved for the treatment of patients with AML.

Evaluating eligibility criteria and scanning electronic health records for eligible patients; AI predicted the likelihood of failure or success in trial. AI systems have also been developed to discover new treatment strategies from genomic data and detected drug-sensitive targets [31-34]. AI techniques were also developed to evaluate patients eligible for transplant and patients at risk of complications before starting treatment [35-37]. Post-transplant recurring was predicted using alternative decision trees [38]. It can also be used to predict the development of acute graft versus host disease after allogeneic transplantation [39, 40)] Many studies have been carried out investigating the use of AI tools to improve hematopoietic cell transplantation (HTC). The choice of transmitter and receiver pairs for HCT is a major issue that can affect the prognosis of HCT recipients. Different studies have investigated the possible use of AI methods and tools to overcome this challenge. Marino [41] and Buturovic [42] used AI methods to identify 19 amino acid substitutes shows bad outcome following HCT. Despite the optimistic preliminary results, these algorithms failed in the validation study. Sarkar and Srivastava have developed an algorithm that uses both HLA and the lethal cell immunoglobulin-like receptor to improve transmitter selection for recipients with acute myelogenous leukemia (AML) [43]. The algorithm was able to increase the accuracy of estimates by 3% - 4% compared to the usual analysis. Sivasankaran et al. proposed a black box model in the development of a system that uses non-secondary HLA features in the selection of donors, but to date, no data has been reported on confirming or improving accuracy [44]. Despite all the advances in HCT, HCT recipients are at risk of many complications that can increase their mortality and morbidity. Therefore, predicting the risk and prognosis of recipients to develop these complications will help clinicians. They can make better decisions that will improve patients' quality of life and quality of survival. In 2015, a prediction model to classify AL patients according to their prognosis following allogenic HKT was developed [45]. The results showed that this method is a valid tool for classifying the risk of AL patients under HCT. The system was able to predict 100 days of mortality, leukemia-free survival, 2 years of overall survival, and relapse mortality. Using pre-transplant minimal residual disease

(MRD), Li et al. predicted the allogenic HCT result in AML and Myelodysplastic syndrome (MDS)[46]. The approach was found to distinguish between abnormal (MDS or AML) and normal cases by 90.8% in the training set and 84.4% in the verification set. System results are interpreted 100 times faster than exports.

In B-cell Acute Lymphoblastic Leukemia, artificial intelligence was used to predict recurrence by analyzing differences in the intensity of marker expression. The prognostic potential of immunophenotypic marker expression density was evaluated. Classifiers have been created to measure the differences between patients with relapse by associating them with genetic information. Thus, the relationship between the sub-expression of the CD38 and the probability of recurring was determined [47].

Recently, automated digital microscopy systems have been developed. They can take advantage of a digital camera connected to a more advanced computer system. Digital images of individual cells are taken. A computer-aided classification based on image analysis parameters of the geometric, color, and tissue properties of the blood cell. Image analysis automates the blood-spreading review process and gives faster slide reviews. Digital image analyzers also let remote networked laboratories quickly transfer images to a central laboratory for review. This simplifies various basic business functions in laboratory hematology such as consultations, digital image archiving, libraries, quality assurance, proficiency assessment, education, and training [48, 49].

Changes in the specific cell population can be detected by using simulation models. Many differential equations are applied for each cellular subspecies or chemical tool during immune interactions. In recent years, tumor complex immune properties such as spatial dynamics of the tumor, cellular heterogeneity, cytokine activity, signaling, and modular factors have been added to these simulation models. Personalized mathematical models have been developed to improve the effectiveness of newly developed immunotherapies during clinical research. AI techniques can facilitate precise planning of treatments for optimization of clinical trials of innovative stem cell and gene theatrics in pediatric patients. Predicting clinical results can simplify patient data [50].

4. Conclusion

AI applications can be used at all stages of patient management in hematology from diagnostic peripheral blood analysis to gene profiling. AI is important for developing individual-specific treatment. Many studies on leukemia classification, stem cell treatments, and genetic programs also continue. As a result, artificial intelligence systems will be used much more in the future than it is now. Models of hematological data supported by intelligent systems will set the stage for us to better understand diseases and develop new treatments.

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