EDITORIAL

ARTIFICIAL INTELLIGENCE IN CARDIOLOGY

"Artificial Intelligence is the new electricity"
Andrew Ng

Traditional medicine was, and still is, based on history, physical signs, routine tests, imaging and molecular data. In each stage of the process for the final diagnosis and the treatment plan medical thinking is a real help. Medical thinking over time has evolved in parallel with the evolution of medical science.

Training for effective medical thinking need years of study, and the elaboration of the diagnosis also consumes time, and in some fields, we need experts (other preparation time, another time to elaborate the diagnosis). Of course, we have to admit that medical thinking has a subjective side.

The great medical achievements of the 20th century was the following: electrocardiogram-1903-Einthoven; cardiac catheterization -1929/1941 – Forssman / Cournand; echocardiography -1954 - Elder and Hertz; coronary angiography -1958-Sones; invasive cardiology -1978 - Gruentzig. Computed tomography, magnetic resonance imaging, optical coherence tomography can be added...

The 21st century, in the first 2 decades, is dominated by two scientific achievements: genetic and artificial intelligence.

What is artificial intelligence?

There are many definitions, but this one seems to be the clearest: "... computer systems performing the tasks that normally require human intelligence" (1).

The avalanche of data, the "flood of data", which exceeds the power of human imagination, is stored by computers with a capacity that is hard to imagine (every day 2.5 exabytes (2.5×10^{18}bytes) are created and can thus be stored over ½ of all the words ever spoken in the whole world (including telephone conversations) (2) .

This data has been called "**big data**". (fig 1)

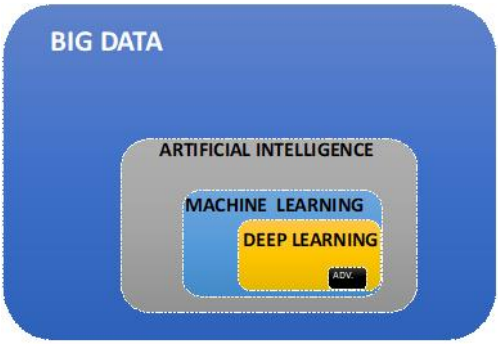

Fig. 1. Components of the artificial intelligence. ADV-advance deep learning

In this „avalanche of data" **Artificial intelligence** (AI), is programmed to imitate human behavior, so AI works with human-made programs and algorithm. Within AI has been developed so called automatic learning, **machine learning**, when computers learn without programs, through examples from the hundreds and thousands of received information (e.g., electrocardiograms, computed tomography or other data).

Here man has only the role of supply of data in the sense that he provides the examples to the system. The human being trains the system, and the system no longer needs programs to function.

Later a complex network of neurons, artificial neurons, was developed, neurons that transmit information from one to another, gathered from the immensity of data, information that they are processed by the artificial neuron network without being understood by human intelligence. This stage is known as **deep learning.**

In deep learning the information collected from different sources enters the system, the information is processed and exchanged with other neurons from many layers and finally conclusions (output) are drawn, and decisions are made (fig. 2).

Conclusions are drawn, quite good, even very good. Nobody knows, nobody understands until today how to get a certain conclusion. For this reason, this part is known as **black box** and creates a big headache for everyone. **As AI becomes more advanced, it is less understood by humans**. Recently a new sub-group called **advanced deep learning** has emerged ! (3).

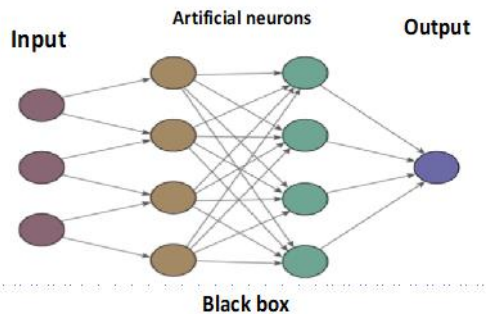

Fig 2. ***Deep learning***. The data entering the system are processed by the neural network and the result is released. It is not known how the result is reached (3)

Although this concept of AI was started in the 1950s by Alan Turing and amplified by Jack Good in the 1970 its development has been done in recent years (because the computers were not up to store and process a big data) with increased velocity (4).

Today AI has 3 major applications in medicine: a) disease prevention and diagnosis; b) faster development of medicines and vaccines (see the anti-COVID-19 vaccine) and c) gene editing.

We will discuss here the relationship between AI and cardiology.

AI has many applications in cardiology in this time and especially in the near future.

Thus, AI can read images or analyses ventricular function, to diagnose valvular heart diseases, arrhythmias, congenital heart diseases reading electrocardiography (fig. 3).

Electrocardiography. Its interpretation can be time-consuming and challenging at times. Automated ECG interpretation is widely used, from many years, with various limitation and over-reading.

Some years ago, in 2002, with my colleague Dr. Ioana Stoian, we have published a book on electrocardiography (5) where one chapter (64 pages), out of the 4 chapters of the book, was dedicated to the electrocardiographic traces read by the computer. We were drawing attention to the erroneous interpretations of computer algorithms and inviting doctors to learn the electrocardiogram well.

Today things are different, apart from the automatic good reading of the electrocardiogram, AI can recognize valvular heart diseases, congenital heart diseases, rhythm disorders, cardiomyopathies and even ventricular function !

Atrial fibrillation is one of the most

common arrhythmias.

Today various mobile devices can be used for detection of atrial fibrillation, these include smartphones, smart bands or smartwatches and earlobe sensors (6).

AI can interpret electrocardiograms during sinus rhythm and was able to find out whether a patient had experienced atrial fibrillation previously and whether it would occur latter (7). This, like other "achievements" of AI, is very curious and still difficult to understand for me.

For many years AI has been a real help in electrophysiology studies.

AI and ECG can recognise left ventricular ejection fraction. Z. Attia *et al.* tested a set of 52.870 patients with ventricular dysfunction (EF <35%), with 12-lead ECG and showed sensitivity 86.3%, specificity 85.7% and accuracy 85.7%. (8).

The ability of the algorithm to read an ECG and see if the FE is low is very important for daily practice, for prevention and for medical research.

Another example: one program was instructed to identify the presence of a low left ventricular ejection fraction from 100,000 ECG (plus other bonus data).

The result was 0.93 (area under the curve), very good! In a recent randomized trial published in Nature Medicine, Yao and colleagues illustrate the power of utilizing AI-enabled ECGs to identify individuals with reduced heart function (9).

Now, using AI-assisted interpretation of ECGs are able to tell us much more. The electrocardiogram with the help of AI can indicate a certain valvular heart disease, for example aortic stenosis (10) mitral stenosis and can evaluate pulmonary hypertension (11, 12) (fig. 3).

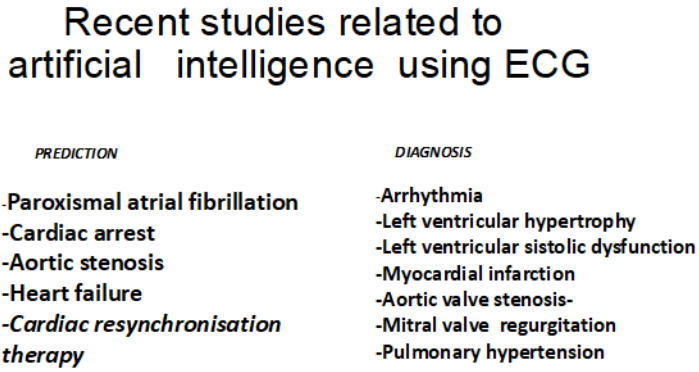

Fig. 3. Recent studies related to artificial intelligence using electrocardiography

Cohen-Shelly *et al.* (10) developed and validated an AI model for detecting aortic stenosis using electrocardiography, they have shown that AI using ECG can identify patients with moderate or severe aortic stenosis and might be able to predict developing aortic stenosis! They have screen ECG and Echo 258,607 patients. In the test group, (102,926 (40%) randomly selected subjects) the AI-ECG patients was positive with the area under the curve of 0.85. The sensitivity, specificity, and accuracy were 78%, 74%, and 74%, respectively (fig. 4).

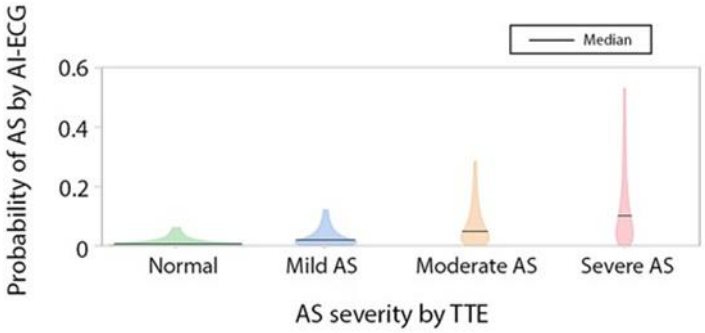

Fig. 4. The probability of aortic stenosis positive labelled by AI-ECG compared with Echo (25) AS-aortic stenosis; TTE- transesophageal echocardiography

Cardiovascular imaging

The first applications of AI in cardiology were possible in digitally acquired images including Echocardiography, Cardiac CT (Computed Tomography) and MRI (Magnetic Resonance Imaging) as well as nuclear imaging (13).

Echocardiography

Echocardiography as a technique has advanced very quickly thanks to computers and advance as an interpretation thanks to artificial intelligence. The results of the echocardiographic examination depend, till now, on the echocardiographer and for this reason this examination has an important subjective part.

Today AI has changed that. Cavity size, wall thickness, ejection fraction and multi-parametric Doppler are automatically calculated and displayed (14).

Now with the aid of AI some diseases are also recognized, such as hypertrophic cardiomyopathy, constrictive pericarditis. Very important for a clinician is the differential diagnosis between constrictive pericarditis and restrictive cardiomyopathy (very difficult diagnosis) and between hypertrophic cardiomyopathy and athletic myocardial hypertrophy.

Cardiac computed tomography (CCT)

CCT is used often for coronary angiography and specially to determine the location and extent of atheromatous plaques in the coronary vasculature as well as for calcium scoring.

Motwani *et al.*, have studied 10,030 patients with suspected coronary artery disease with CT angiography and follow-up the patients during a 5-years. 25 clinical and 44 CT angiography parameters were measured. The AI approach was a significantly better predictor of a 5-year mortality, in comparison to the clinical or CT angiography alone (16).

Recently, in a multicenter study, was developed and validated a deep system for measures of plaque volume and stenosis severity (17). Another research has been used AI for automatic estimation of CT coronary angiography fractional flow reserve (FFR) with good agreement between AI derived values and those which were invasively measured (18).

Cardiac Magnetic Resonance (CMR) is used for the diagnosis of cardiomyopathies, congenital heart disease, valvular heart disease, ischemic heart diseases, pericardial lesions, and cardiac tumors. AI can help to a more efficient scanning and accurate interpretation process: image construction,

image segmentation and image quality control (19).

In a recent trial of 1,348 patients with hypertrophic cardiomyopathy, a new AI driven CMR technology named virtual native enhancement (VNE), was used to generate images identical to the standard Late Gadolinium Enhancement (LGE), without the need of a gadolinium-based contrast agent. VNE resembles conventional LGE but does not require intravenous access or administration of contrast ! (20).

*Cardiac resynchronization therapy (CRT***)**

Conventionally, patients eligible for CRT implantation have greater benefit on reduction of mortality and should have an ECG morphology with Left Bundle Branch Block and QRS duration ≥ 150 ms. Around 30% of patients meeting these criteria and receiving an implant, do not experience clinical benefit from CRT. A model, with the aid of AI, for better discrimination of the risk (mortality) were developed for prediction of evolution post-CRT and with a 2-fold change in survival (21).

Other applications

An algorithm for heart murmur detection was developed: pathologic cases were identified with sensitivity of 93%, specificity of 81%, and accuracy of 88%. AI has a potentially useful screening tool for valvular heart disease in a general population.

A recent interesting example: a group of Chinese scientists developed a convolutional neural network (CNN) which can detect coronary artery stenosis > 50%, (stenosis documented by angiography)), *via* analyzing the patient's facial photo (!) to 5,796 patients with an 85% sensitivity and 54% specificity (higher than the standard prediction scores) (22).

Single-photon emission computed tomography (SPECT) stress testing. AI methodology has been applied in this modality, to improve image acquisition, image reconstruction and automated quantitation (3)

I would like to make a clarification here. I don't want it to be remembered that I have unlimited confidence in AI, that all the data is correct, unchangeable. I am convinced that AI brings support to our activity, to life in general and to medicine in particular, but we must be careful about limits, exaggerations, dysfunctionalities and the impact on people and, in our case, on doctors. AI should act to support and not replace the physician, but as Erick Topol says that "doctors who will use new technologies & AI will replace doctors who will not use it" (23)

Remains to be discussed who is responsible for the AI wrong results.

The application of AI in Cardiology is still in its infancy. It is expected clinical validation, implementation as well as regulation. Food and Drug Administration (FDA) has released a regulatory framework to establish safe and effective AI- based medical devices. (24). The European Union has also proposed a regulatory framework on the use of AI - technology (25).

In the future, AI will have an important role in the prevention of diseases and in the treatment of the diseases as early and efficiently as possible.

Cardiologists should educate themselves in the development of AI and utilize them in their practice.

There are many ongoing studies/trials regarding AI and cardiology in different fields such as: preventive cardiology, cardiovascular imaging, electrocardiography, heart failure, interventional cardiology and we are waiting for the results in the follow-

ing years (26)

The role of doctor in the era of AI

Doctors will have to remain the ones to make the final decision

For patients doctors will provide explanations, humanity, empathy.

The question is whether in the future will be better than today? Possible, if we consider that the medical error is a third cause of death after cardiovascular diseases and cancer (27)

In conclusion, medical thinking still proves its value, and we have an obligation to develop it and induce it to the younger generations.

It is clear that AI exhibits significant potential in the field of cardiology, it can improve diagnostic accuracy and support clinical decisions for many diseases.

Artificial intelligence in the future will be an integral part of medicine.

It is important to prepare the new generation of doctors and the new generation of teachers regarding the concept of AI and the usefulness of this concept.

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