Journal of
Transcatheter Interventions
e-ISSN e-2595-4350

Artificial intelligence in coronary physiology: where do we stand?

Inteligência artificial na fisiologia coronária: onde estamos?

Rohit Mody[1iD], Debabrata Dash[2iD], Deepanshu Mody[3iD]

[1] Department of Cardiology, MAX Super Specialty Hospital, Bathinda, Punjab, India.
[2] Department of Cardiology, Aster Hospital, Mankhool, Dubai, Al Quasis, United Arab Emirates.
[3] Department of Biological Sciences, Purdue University, West Lafayette, United States.

DOI: 10.31160/JOTCI202230A20220009

ABSTRACT - The use of invasive coronary physiology to select individuals for coronary revascularization has been established in current guidelines for the management of stable coronary artery disease. Compared to angiography alone, coronary physiology has been proven to improve clinical outcomes and cost-effectiveness in the revascularization process. Randomized controlled trials, however, have questioned the efficacy of ischemia testing in selecting individuals for revascularization. After an angiographically successful percutaneous coronary intervention, 20 to 40% of patients experienced persistent or recurrent angina. Artificial intelligence is defined as the usage of various algorithms and computational concepts to perform the complex tasks in an efficient manner. It can be classified into two types: unsupervised and supervised approaches. Supervised learning is majorly used for the regression and classification tasks, and in this optimized mapping between output variables and paired input is carried out to perform the tasks. In contrast to this, unsupervised learning works in the different manner. In unsupervised learning, output variables data is not available and further clusters and relations between input data are found out by using the various algorithms. To acquire more abstract representation of data, deep learning technology, which uses the multilayer neural networks, dominates the artificial learning nowadays.

Keywords: Artificial intelligence; Coronary artery disease; Physiology; Percutaneous intervention coronary; Algorithms

RESUMO - O uso da fisiologia coronariana invasiva na seleção de indivíduos para revascularização coronariana foi estabelecido nas orientações atuais para manejo da doença arterial coronariana estável. Em comparação com a angiografia isolada, a fisiologia coronariana provou melhorar os resultados clínicos e a relação custo-efetividade no processo de revascularização. Ensaios controlados randomizados, no entanto, questionaram a eficácia do teste de isquemia na seleção de indivíduos para revascularização. Após uma intervenção coronária percutânea com sucesso angiográfico, 20 a 40% dos pacientes apresentaram angina persistente ou recorrente. A inteligência artificial é definida como o uso de vários algoritmos e conceitos computacionais para realizar tarefas complexas de maneira eficiente. Pode ser classificada em dois tipos: abordagens não supervisionadas e supervisionadas. O aprendizado supervisionado é usado principalmente nas tarefas de regressão e classificação, e nele é realizado um mapeamento otimizado entre variáveis de saída e entrada pareadas para executar as tarefas. Em contraste com isso, o aprendizado não supervisionado funciona de maneira diferente. Nesse aprendizado, os dados das variáveis de saída não estão disponíveis, e outros *clusters* e relações entre os dados de entrada são descobertos, usando-se vários algoritmos. Para se adquirir uma representação mais abstrata dos dados, a tecnologia de aprendizado profundo que utiliza as redes neurais multicamadas domina o aprendizado artificial atualmente.

Descritores: Inteligência artificial; Doença da artéria coronariana; Fisiologia; Intervenção coronária percutânea; Algoritmos

How to cite this article:
Mody R, Dash D, Mody D. Artificial intelligence in coronary physiology: where do we stand? J Transcat Intervent. 2022;30:eA20220009. https://doi.org/10.31160/JOTCI202230A20220009

Corresponding author
Rohit Mody
MAX Super Specialty Hospital
Mansa Rd, Guru Ki Nagri, Bathinda
Zip code: 151001 – Punjab, India
E-mail: drmody_2k@yahoo.com

Received on:
Jul 20, 2022

Accepted on:
Oct 11, 22

INTRODUCTION

Despite the rapid advancement of technology, each major breakthrough has the potential to transform a wide range of facets of civilization.[1,2] Miniaturized technologies and smartphone apps have made it an ordinary practice to receive constant streams of personalized information.[3,4] Artificial intelligence (AI) in medicine, particularly in cardiovascular imaging, also has enormous potential.[2,5,6] Imaging technologies allow us to obtain unlimited information about the structure and function of the heart.[7]

Imaging methods have also grown dramatically in tandem with the technological revolution.[5,8] Existing procedures are given new parameters, allowing researchers to learn more about the heart performance.[7,9,10] Are more data points advantageous if they cannot be utilized in clinical practice?[11] Prioritizing the information needed for medical management is preferable to having an overabundance of data points.

Using AI in cardiovascular imaging helps bridge the gap between new technology and massive data.[12-14] In cardiovascular imaging, machine learning (ML), a branch of AI, is particularly relevant since it can analyze vast volumes of information in a variety of ways.[1,15,16] Machine learning can bring together data from a range of sources and display it in a way that is useful to the practitioner.[13,14] Automated measurements in multiple imaging modalities can also be performed by the system.[17,18] Precision medicine will benefit from the rise of AI. Artificial intelligence and machine learning in cardiovascular imaging are discussed in this review article.

LIMITATIONS OF FRACTIONAL FLOW RESERVE PULLBACK

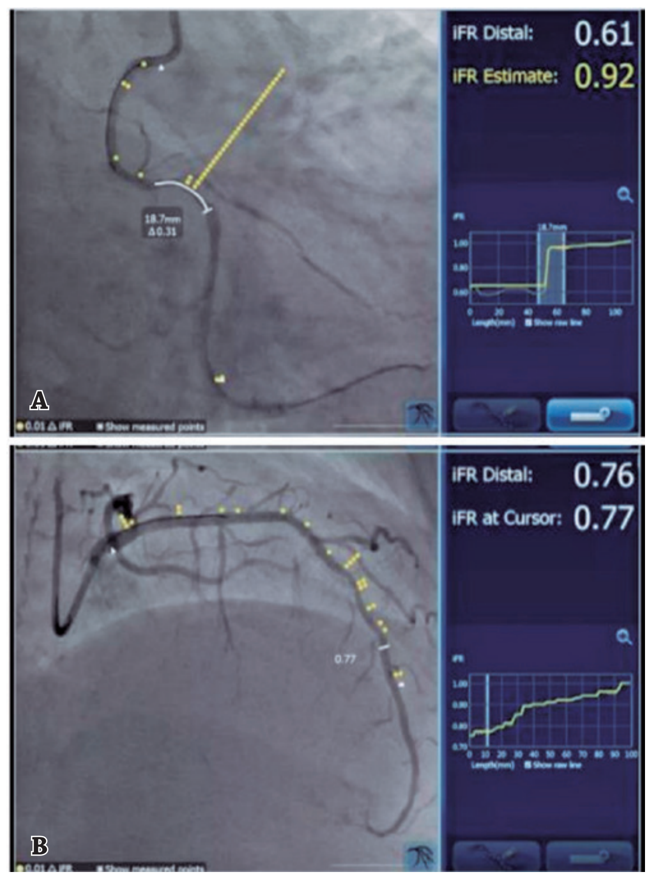
Cross-talk between several stenoses or extensive illness in the same vessel limits the use of fractional flow reserve (FFR) for pressure wire pullback. Due to the hemodynamic properties of a subsequent stenosis restricting the maximum flow across a single stenosis in the presence of persistent hypertension, it is common for clinicians to grossly underestimate the true severity of each stenosis.[19,20] Hyperemic flow and, thus, the pressure drop across the second stenosis will increase once one stenosis is corrected. For pullback assessments, FFR is less suitable because of these hemodynamic properties, especially in tandem stenoses or diffusely damaged arteries.

INSTANTANEOUS WAVE-FREE RATIO PULLBACK WITH CO-REGISTRATION

As stenosis severity increases, coronary flow is maintained until the channel is almost totally blocked under resting conditions.[21] In such conditions and no prior hyperemia, the pressure wire pullback assessment is less susceptible to hemodynamic dependency between successive stenoses within a single artery.

Relatively simple resting indexes such as instantaneous wave-free ratio (iFR), which are determined on a beating basis, provide for a high-resolution physiological map during the pullout of pressure wires.[22] Instantaneous wave-free ratio pullback can guide intervention by emphasizing stenosis that provides the highest pressure drop inside the artery, through quantification of the pressure gradient at each point in the vessel. Using this technology to avoid the stenting of vessels that do required implants, but appear significant on an angiogram is equally critical. Thus, the iFR pullback allows the coronary artery disease (CAD) pattern to be described as focused, diffuse, or a mixture of them.

It is now possible to trace the flow of the pressure wire through the vessel in real-time under continuous fluoroscopy in the next generation of this technique, iFR co-registration. The pressure drop at any specific stenosis can be visualized on the patient's angiogram, using data from an iFR pullback maneuver that has been co-registered with the coronary angiography (Figure 1A).[23] Another benefit of using iFR is the ability to construct unique stenting procedures to accurately anticipate post-percutaneous coronary



Source: Al-Lamee et al.[23]
iFR: instantaneous wave-free ratio.
Figure 1. Instantaneous wave-free ratio co-registration images. The yellow dots overlying each angiogram correspond to the location of a 0.01 instantaneous wave-free ratio pressure drop. (A) A focal stenosis in the right coronary artery. The operator has specified the planned stented segment, which results in a predicted physiological gain of 0.31 instantaneous wave-free ratio unit, resulting in an estimated post-percutaneous coronary intervention instantaneous wave-free ratio of 0.92 for the vessel. (B) A diffusely diseased left anterior descending artery. The cursor may be moved to any given location in the vessel to determine the estimated instantaneous wave-free ratio at that position.

intervention physiological outcomes. Operators can now plan their preferred stenting method to maximize the physiological gain per stented segment (Figure 1B).[23]

Several areas of cardiology, including coronary physiology, have experienced an increase in the prominence of AI. Due to signal drift or aberrant waveforms, roughly 30% of coronary physiology data is discarded following core laboratory assessment.[24] Artificial intelligence has been proposed as a method to detect irregular waveforms in real-time and inform interventionists. Damping can be detected quickly and accurately (98.7% to 99.4% accurate) by utilizing neural networks for arterial waveform analysis, demonstrating how machine learning can help ensure the quality and safety of normal clinical practice.[25] To find out whether neural networks can be taught to advise optimal revascularization sites based on physiological and pullback data, more research is needed.

Novel physiological evaluation approaches that do not require the addition of pharmacology or the use of a coronary wire are also something we expect to become standard practice in the near future, since they will benefit the user experience as well as the overall quality of care. FFR employs a three-dimensional angiographic reconstruction of the stenosed conduit and the contrast flow frame count to estimate the quantitative flow reserve (QFR). Studies have demonstrated that QFR can detect functionally substantial stenosis,[26] and that post-percutaneous coronary intervention (PCI) QFR may have predictive significance.[27,28] These novel methods, in conjunction with FFR-computed tomography (CT),[29] may enable a less risky evaluation of CAD from anatomical and physiological perspectives.

When evaluating prognostic endpoints, it is important to keep in mind that many cardiac events arise from non-significant lesions angiographically or physiologically. Non-culprit coronary lesions with high-risk features, such as thin-cap fibroatheromas or large plaque volumes, were found to be the majority of those responsible for major adverse cardiac events following acute coronary syndrome (ACS), according to the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study.[30] More recent studies have shown the utility of intravascular imaging, including near-infrared spectroscopy (NIR), for identification of vulnerable lipid-rich plaques (LRP) that may be physiologically non-flow-limiting, but pose a high risk of rupture in the coronary tree, combined with a randomized, controlled, intervention trial (PROSPECT ABSORB).[31,32] Further research is warranted to discover whether or not treating these LRP in advance can lead to better clinical outcomes. As a result of these findings, the development of clinical techniques to detect susceptible plaques is essential for real progress toward the goal of reducing cardiac risk by revascularization. Prognostic endpoints in patients with stable CAD can be improved using these technologies in conjunction with the best possible medical treatment.

TECHNICAL CONSIDERATIONS

Pitfalls in physiological assessments

Prior to or following a PCI procedure, precise physiological measurements may only be made by adhering to a certain set of guidelines. It is common to run across problems with determining the best assessment method, but most of these issues may be readily fixed. For any physiological evaluation, the most prevalent errors, their repercussions, and methods for correcting them are outlined in table 1 and figure 2.

Technical considerations specific to post-percutaneous coronary intervention physiological assessments

As the vessel reacts to stenting, it is usual for patients to experience coronary vasospasm after PCI. Following PCI, intracoronary nitrates should be administered before repeating a physiological evaluation, regardless of the method used.

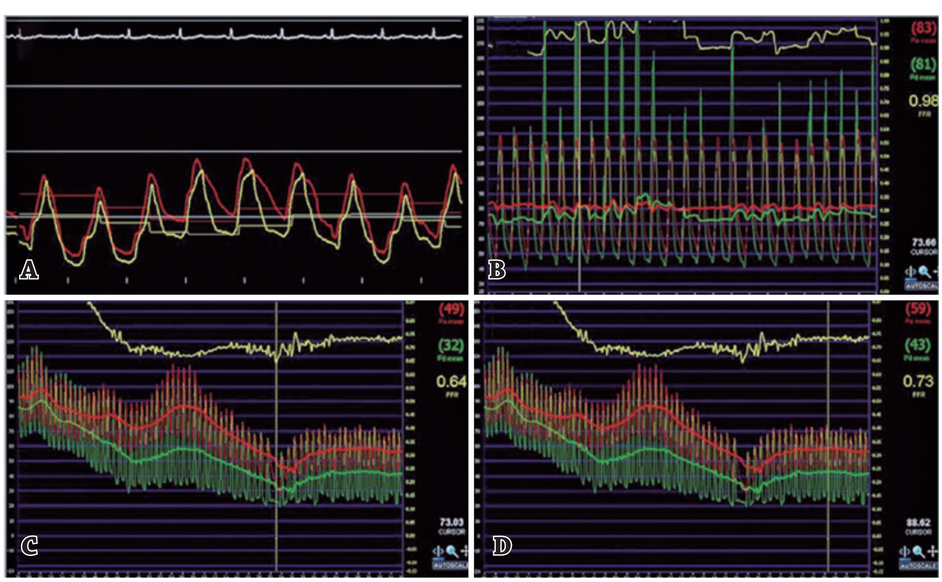
Pressure wire advancement may be difficult in the post-PCI context, especially in more intricate stented segments. A good method is to run the pressure wire alongside the workhorse wire. Consider the possibility of advancing a pressure wire through hidden ruptures or dissections, which may not be visible angiographically if the post-PCI haziness is severe. There may be an advantage to the use of a dual lumen catheter for wire exchange distal to stenting, although dampening of the proximal aortic pressure through the guide catheter reduces this technique's accuracy. Dedicated microcatheter-based pressure sensors are now in use, although the system overestimates lesion severity due to a pressure impact caused by the catheter across the vascular segment under assessment.[33] Over-the-wire microcatheters can be utilized to replace the workhorse wire with a pressure wire, and a trapping balloon technique can be used to separate the microcatheter from the guiding catheter to avoid these causes of error. This more complicated solution is helpful in ensuring accurate hemodynamic readings.

Preliminary research focused on the validity of non--hyperemic pressure ratio (NHPR) following PCI. Following PCI balloon inflation, there is a potential for an extended period of hyperemia. Resting circumstances must be restored before NHPR measurement to avoid persistent hyperemia, which reduces the NHPR value. Hyperemia following coronary blockage only lasts about 1 minute, on average, according to current findings.[34] As a result, resting conditions are often recovered in the time it takes to conduct post-PCI physiological tests.

Table 1. Common pitfalls in physiological assessment technique and resolution methods

Pitfall in assessment	Technique description	Physiological result	Resolution aim
Omission of therapeutic heparin dose	Subtherapeutic anticoagulation prior to instrumentation of coronary artery	Thrombus formation in catheter or on pressure wire	Ensure therapeutic dose unfractionated heparin administration for every pressure wire assessment
Omission of intracoronary nitrates	Spasm of coronary artery during instrumentation	↓Pd=↓FFR Stenosis severity overestimated	Intracoronary bolus glyceryl trinitrate titrated to blood pressure prior to normalization
Failure to perform normalization	Poor calibration of Pa and Pd trace	Fixed error in Pd/Pa ratio	Normalize every assessment and ensure Pd/Pa=1.00 before passing wire distally
Failure to remove needle introducer	Presence of the needle introducer in the hemostatic valve precludes accurate Pa assessment	Needle introducer ↓Pa=↑FFR Stenosis severity underestimated	Always remove needle introducer prior to normalization, and again prior to measurement of FFR
Damped Pa trace	Guiding catheter "wedged" trace occurs when the guiding catheter position abuts the arterial wall	↓Pa=↑FFR Stenosis severity underestimated	Ensure coaxial catheter position, use smaller guiding catheter
Ostial stenosis	Ventricularization of Pa trace due to catheter damping in presence of ostial stenosis	↓Pa=↑FFR Stenosis severity underestimated	Retract catheter into aorta. Perform normalisation with pressure sensor in aorta
Use of side hole catheter	Pa inaccurately measured due to the presence of side holes in the aortic root	↑Pa=↓FFR Stenosis severity overestimated	Do not use side hole catheter for physiological assessments
Whipping artefact	During systole, the pressure wire contacts the arterial wall creating Pd artefact	↑Pd=↑FFR Stenosis severity underestimated	Easily recognized, retract or advance several millimeters to new position and retest
Wire signal drift	Development of piezoelectric pressure sensor electronic signal offset during assessment	Inaccurate FFR measurement in either direction. Stenosis severity underestimated or overestimated	Always perform a "drift check". Where Pd/Pa falls outside 1.00±0.02, re-normalize and repeat assessment
Incorrect FFR assessment point	Consoles typically report the lowest Pd/Pa measured, but FFR should be measured at stable hyperemia	↓FFR Stenosis severity overestimated	Manually adjust the FFR assessment point to the period of stable hyperemia

Source: Al-Lamee et al.[23]
Pd: resting distal coronary pressure; FFR: fractional flow reserve; Pa: normal aortic pressure.



Source: Al-Lamee et al.[23]

Figure 2. Pitfalls in the assessment of coronary physiology. (A) Example of damped normal aortic pressure trace with a characteristic waveform. (B) Example of whipping artefact. (C) Example of an incorrect cursor position to measure fractional flow reserve. The console may default measurement to the lowest resting distal coronary pressure/normal aortic pressure value. However, this position does not correspond to stable hyperemia and will overestimate stenosis severity. (D) The cursor has now been adjusted to ensure that fractional flow reserve is measured at a period of stable hyperemia.

The goals of post-PCI physiological assessment are to determine a suboptimal hemodynamic result and, secondly, to identify the root cause. For the first aim, we believe that either an FFR or an NHPR could be utilized based on the provided data. To further understand the underlying mechanism of post-PCI ischemia, an NHPR is more suited for pullback and co-registration in these cases. Using a hyperemic pressure ratio for pullback assessments in the post-PCI scenario may be prone to the same constraints as in the pre-PCI setting, namely hemodynamic cross-communication between sick segments of the same channel.[20]

BASIC CONCEPT OF ARTIFICIAL INTELLIGENCE IN CLINICAL MEDICINE

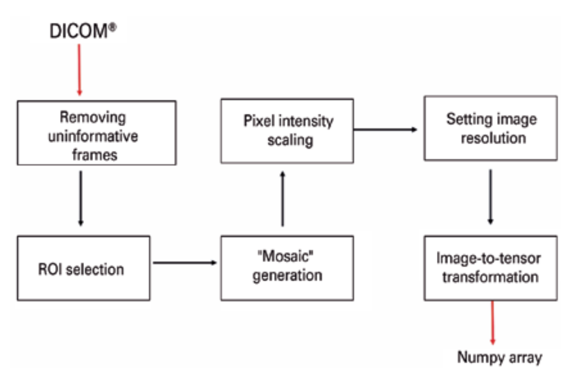
Massive growth has been achieved by the AI industry in various fields, including medicine in the past decade. Artificial intelligence works from two prospective along with mathematics and computer science,[35] which are the development of algorithms[36] and high yield computing infrastructure.[37] Artificial intelligence work in various other fields with much sharper capabilities in digital storage, computing power and data collection. These days technology that potentiates the speed and breadth of knowledge and information helps in the development of AI. Development in technology helps in development of AI algorithm, which further enables collection of a large amount of data.

In the early stages of AI in the medical field, it mainly focused on computer and electronic controls of medical tasks; however, recently it is more focused on prognosis and risk prediction. Various studies have demonstrated the role of AI in daily basis activities for assisting clinicians in their work for diagnosis, reporting and prognosis. But most AI applications are not used regularly in clinical practice rather they are more useful for research purposes. Some successful implementation has been seen and a list of all Food and Drug Administration (FDA) cleared AI algorithms for radiology was published by the Data Science Institute of the American College of Radiology. Some AI applications are not useful for clinical purposes.[38,39] For example, Zech et al. worked on convolutional neural networks (CNN) across their pneumonia screening and they concluded data produced by CNN is worse compared to others.[38] For implementation and acceptance of AI in the medical field, proper assessment is required in the clinical setting.

Artificial intelligence algorithm validation was evaluated by Kim et al. and published in AI research papers for different medical fields, like dermatology, pathology and radiology.[39] They reported that for the assessment of AI applications, only 6% of studies used external validations.[39] For improvement in the validation of AI algorithms in medical fields, several guidelines have been published.[40] Nowadays, for validation of AI algorithms externally, many papers have been published.[41] Along with this, proper implementation of several guidelines is the topical need for the protection of patient privacy and cyber security, which further creates awareness and shares information among clinicians for promoting AI application acceptance.

A white paper on AI was released by the European commission in February 2020, and provides information about the guidelines for use of AI applications in medical fields.[42] These European Union guidelines provide a high level of protection of patient privacy and cyber security through medical device and data protection laws. They further asked for the addition of some specific regulations, such as the need for training, data, maintenance of records, accuracy, transparency, and revaluation by humans. FDA also released some statements for use of AI in medical fields. Quantifications of applications by medical assistance and medical data clinical interpretation applications by medical require more elaborated FDA approval.[43]

Along with some legal activities for medical AI, a significant role is also played by certain ethical frameworks.[44] Some issues, such as gender, race, and economical aspects, should be evaluated and discussed together with the implantation of medical data. Risk prediction and prognosis should be evaluated with AI for limiting options and health insurance coverage in some groups of patients. It is necessary to learn to maintain the proper balance between risks and benefits equally when using AI. The joint European and American multi-society task force goes through these issues and states that AI implementation in the medical field requires more research.[45] Figure 3 shows the process of Digital Imaging and Communications (DICOM®) image elaboration for the development of the deep learning algorithm.[46]



Source: Muscogiuri G, Assen M, Tesche C, Cecco CN, Chiesa M, Scafuri S, et al. Artificial Intelligence in Coronary Computed Tomography Angiography: From Anatomy to Prognosis. Hindawi. BioMed Research International. 2020. https://doi.org/10.1155/2020/6649410. Figure 1: Streamline used for the development of images useful for DL algorithm starting from DICOM images; p. 3.[46]
ROI : region of interest.
Figure 3. Starting with Digital Imaging and Communications pictures, this pipeline was utilized to create images appropriate for the deep learning algorithm.

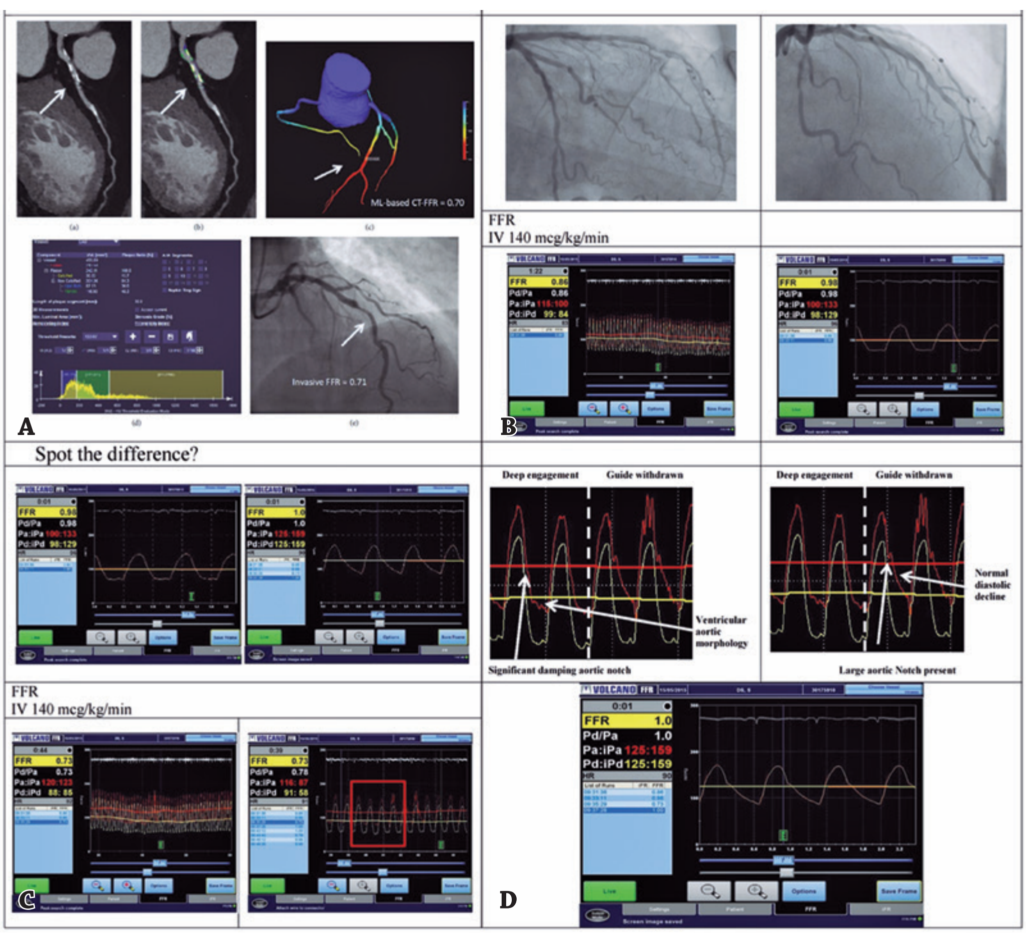
ARTIFICIAL INTELLIGENCE IN THE EVALUATION OF ISCHEMIA BY USING THE VARIOUS IMAGING METHODS

At present, progress and research in AI applications are implemented for the assessment of CT-derived myocardial ischemia. For observation of hemodynamically significant CAD, most of the AI applications published use CT-perfusion. Only one vendor provides ML solutions concerning CT-FFR.[47] Lately, Keya Medical, from Beijing, China, announced a software application that is commercially available.[48]

Machine learning-based CT-FFR uses multilayer neural network which uses a virtual dataset of 12,000 synthetic three dimensional coronary models against the computational fluid dynamics (CFD) approach.[49] Several single-center and one multicenter trial were organized for clinical validation of the ML approach, to assess lesion-specific ischemia along with invasive coronary angiography and coronary CT angiography. A representative case is shown in figure 4.

Application of AI provides identification of perfusion defects and myocardial segmentation through CT-perfusion. By usage of different ML approaches, introductory results have shown an appropriate use criteria of 0.73 for automated segmentation, when compared to manual segmentation by the skilled professional reader.[49]

Of all physiology measurements 30% are unsuitable for interpretation. Physiological guidance by AI can help in signal stability, pressure drift and pullback pattern recognition. The development of smart monitoring devices based upon artificial intelligence and various parameters in these devices can be considered, so that it is able to recognize several physiological waveforms. Artificial intelligence works



Source: the authors.
FFR: fractional flow reserve; IVUS: intravenous.
Figure 4. Coronary computed tomography angiography in a coronary artery disease patient. (A) Curved multiplanar reformations created automatically revealing more than 50% stenosis of the proximal left anterior descending artery (arrow). (B and D) The primarily calcified makeup of the atherosclerotic plaque is demonstrated by color-coded computerized plaque assessment of the lesion. (C) The computed tomography-fractional flow reserve value of 0.70 on the three dimensional color-coded mesh indicates ischemia of the underlying stenosis (arrow). (D) With an fractional flow reserve of 0.70, invasive coronary angiography confirms obstructive stenosis of the left anterior descending artery (arrow).

by combining a large set of data to a system, and then using the various algorithms to process data. Before combining the data, developing a comprehensive data set is the initial step, further tutoring the artificial intelligence on what is a beat, and also guide it about which several distinct types of beats are crucial steps.

CONCLUSION

Artificial intelligence is fetching a progressively essential role in the healthcare system. Earlier, it had a role in the processing of static images and the quality of care in clinical settings. For the revolution of health data science across the industry, academia, and national health services, growing the intrasectoral support is beneficial for cardiologists who have a huge interest in artificial intelligence. To potentiate the growth of advanced healthcare analytics, an independent organization named Health Data Research UK is working to bring funders and researchers together. Recently, to empower the responsible research at a large scale by the usage of advanced analytical methods and diverse cardiovascular data resources, an announcement has been made by the British Heart Foundation to do a partnership with Health Data Research UK. Such types of initiatives can foster the biomedical research by providing an opportunity to efficiently access clinical data of good quality at a huge scale.

ACKNOWLEDGMENT

To Ms. Nikita and Rohit Kumar, for assisting finalizing the research article. Figures were edited by Jiwan Singh.

SOURCE OF FINANCING

None.

CONFLICTS OF INTEREST

The authors declare there are no conflicts of interest.

CONTRIBUTION OF AUTHORS

Conception and design of the study: RM, DD and DM; data collection: RM, DD and DM; data interpretation: RM, DD and DM; text writing: RM, DD and DM ; approval of the final version to be published: RM, DD and DM .

REFERENCES

1. Johnson KW, Torres Soto J, Glicksberg BS, Shameer K, Miotto R, Ali M, et al. Artificial intelligence in cardiology. J Am Coll Cardiol. 2018;71(23):2668-79. https://doi.org/10.1016/j.jacc.2018.03.521
2. Sengupta PP, Shrestha S, Berthon B, Messas E, Donal E, Tison GH, et al. Proposed Requirements for Cardiovascular Imaging-Related Machine Learning Evaluation (PRIME): a checklist: Reviewed by the American College of Cardiology Healthcare Innovation Council. JACC Cardiovasc Imaging. 2020;13(9):2017-35. https://doi.org/10.1016/j.jcmg.2020.07.015
3. Seetharam K, Kagiyama N, Sengupta PP. Application of mobile health, telemedicine and artificial intelligence to echocardiography. Echo Res Pract. 2019;6(2):R41-52. https://doi.org/10.1530/ERP-18-0081
4. Magnani JW, Mujahid MS, Aronow HD, Cené CW, Dickson VV, Havranek E, et al.; American Heart Association Council on Epidemiology and Prevention; Council on Cardiovascular Disease in the Young; Council on Cardiovascular and Stroke Nursing; Council on Peripheral Vascular Disease; Council on Quality of Care and Outcomes Research; and Stroke Council. Health Literacy and Cardiovascular Disease: Fundamental Relevance to Primary and Secondary Prevention: A Scientific Statement From the American Heart Association. Circulation. 2018;138(2):e48-e74. https://doi.org/10.1161/CIR.0000000000000579
5. Dey D, Slomka PJ, Leeson P, Comaniciu D, Shrestha S, Sengupta PP, et al. Artificial intelligence in cardiovascular imaging: JACC state-of-the-art review. J Am Coll Cardiol. 2019;73(11):1317-35. https://doi.org/10.1016/j.jacc.2018.12.054
6. Al'Aref SJ, Anchouche K, Singh G, Slomka PJ, Kolli KK, Kumar A, et al. Clinical applications of machine learning in cardiovascular disease and its relevance to cardiac imaging. Eur Heart J. 2019;40(24):1975-86. https://doi.org/10.1093/eurheartj/ehy404
7. Shrestha S, Sengupta PP. Imaging heart failure with artificial intelligence: improving the realism of synthetic Wisdom. Circ Cardiovasc Imaging. 2018;11(4):e007723. https://doi.org/10.1161/CIRCIMAGING.118.007723
8. Collet C, Penicka M. Integrating patient-specific information in the noninvasive quest for the vulnerable patient. JACC Cardiovasc Imaging. 2019;12(10):1998-9. https://doi.org/10.1016/j.jcmg.2018.10.025
9. Shrestha S, Sengupta PP. The mechanics of machine learning: from a concept to value. J Am Soc Echocardiogr. 2018;31(12):1285-7. https://doi.org/10.1016/j.echo.2018.10.003
10. Nolan MT, Thavendiranathan P. Automated quantification in echocardiography. JACC Cardiovasc Imaging. 2019;12(6):1073-92. https://doi.org/10.1016/j.jcmg.2018.11.038
11. Sengupta PP, Adjeroh DA. Will artificial intelligence replace the human echocardiographer? Circulation. 2018;138(16):1639-42. https://doi.org/10.1161/CIRCULATIONAHA.118.037095
12. Seetharam K, Shrestha S, Sengupta PP. Artificial intelligence in cardiovascular medicine. Curr Treat Options Cardiovasc Med. 2019;21(6):25. https://doi.org/10.1007/s11936-019-0728-1
13. Min JK. Chess and coronary artery ischemia: clinical implications of machine-learning applications. Circ Cardiovasc Imaging. 2018;11(6):e007943. https://doi.org/10.1161/CIRCIMAGING.118.007943
14. Sengupta PP, Shrestha S. Machine learning for data-driven discovery: the rise and relevance. JACC Cardiovasc Imaging. 2019;12(4):690-2. https://doi.org/10.1016/j.jcmg.2018.06.030
15. Pennell D, Delgado V, Knuuti J, Maurovich-Horvat P, Bax JJ. The year in cardiology: imaging. Eur Heart J. 2020;41(6):739-47. https://doi.org/10.1093/eurheartj/ehz930
16. Singh A, Falk RH. 'A new staging system for cardiac transthyretin amyloidosis': is it already on the verge of obsolescence? Eur Heart J. 2018;39(30):2807-9. https://doi.org/10.1093/eurheartj/ehx740
17. Seetharam K, Shresthra S, Mills JD, Sengupta PP. Artificial intelligence in nuclear cardiology: adding value to prognostication. Curr Cardiovasc Imaging Rep. 2019;12(5):14. https://doi.org/10.1007/s12410-019-9490-8
18. van Assen M, Cornelissen LJ. Artificial intelligence: from scientific curiosity to clinical precocity? JACC Cardiovasc Imaging. 2020;13(5):1172-4. https://doi.org/10.1016/j.jcmg.2019.09.008

19. De Bruyne B, Pijls NH, Heyndrickx GR, Hodeige D, Kirkeeide R, Gould KL. Pressure-derived fractional flow reserve to assess serial epicardial stenoses: theoretical basis and animal validation. Circulation. 2000;101(15):1840-7. https://doi.org/10.1161/01.cir.101.15.1840
20. Nijjer SS, Sen S, Petraco R, Escaned J, Echavarria-Pinto M, Broyd C, et al. Pre-angioplasty instantaneous wave-free ratio pullback provides virtual intervention and predicts hemodynamic outcome for serial lesions and diffuse coronary artery disease. JACC Cardiovasc Interv. 2014;7(12):1386-96. https://doi.org/10.1016/j.jcin.2014.06.015
21. Gould KL, Lipscomb K, Calvert C. Compensatory changes of the distal coronary vascular bed during progressive coronary constriction. Circulation. 1975;51(6):1085-94. https://doi.org/10.1161/01.cir.51.6.1085
22. Nijjer SS, Sen S, Petraco R, Mayet J, Francis DP, Davies JE. The Instantaneous wave-Free Ratio (iFR) pullback: a novel innovation using baseline physiology to optimise coronary angioplasty in tandem lesions. Cardiovasc Revasc Med. 2015;16(3):167-71. https://doi.org/10.1016/j.carrev.2015.01.006
23. Al-Lamee R, Rajkumar CA, Ganesananthan S, Jeremias A. Optimising physiological endpoints of percutaneous coronary intervention. EuroIntervention. 2021;16(18):e1470-83. https://doi.org/10.4244/EIJ-D-20-00988
24. Matsumura M, Johnson NP, Fearon WF, Mintz GS, Stone GW, Oldroyd KG, et al. Accuracy of fractional flow reserve measurements in clinical practice: observations from a core laboratory analysis. JACC Cardiovasc Interv. 2017;10(14):1392-401. https://doi.org/10.1016/j.jcin.2017.03.031
25. Howard JP, Cook CM, van de Hoef TP, Meuwissen M, de Waard GA, van Lavieren MA, et al. Artificial intelligence for aortic pressure waveform analysis during coronary angiography: machine learning for patient safety. JACC Cardiovasc Interv. 2019;12(20):2093-101. https://doi.org/10.1016/j.jcin.2019.06.036
26. Xu B, Tu S, Qiao S, Qu X, Chen Y, Yang J, et al. Diagnostic accuracy of angiography-based quantitative flow ratio measurements for online assessment of coronary stenosis. J Am Coll Cardiol. 2017;70(25):3077-87. https://doi.org/10.1016/j.jacc.2017.10.035
27. Kogame N, Takahashi K, Tomaniak M, Chichareon P, Modolo R, Chang CC, et al. Clinical implication of quantitative flow ratio after percutaneous coronary intervention for 3-vessel disease. JACC Cardiovasc Interv. 2019;12(20):2064-75. https://doi.org/10.1016/j.jcin.2019.08.009
28. Biscaglia S, Tebaldi M, Brugaletta S, Cerrato E, Erriquez A, Passarini G, et al. Prognostic value of QFR measured immediately after successful stent implantation: the international multicenter prospective HAWKEYE study. JACC Cardiovasc Interv. 2019; 12(20):2079-88. https://doi.org/10.1016/j.jcin.2019.06.003
29. Tanigaki T, Emori H, Kawase Y, Kubo T, Omori H, Shiono Y, et al. QFR versus FFR derived from computed tomography for functional assessment of coronary artery stenosis. JACC Cardiovasc Interv. 2019;12(20):2050-9. https://doi.org/10.1016/j.jcin.2019.06.043
30. Stone GW, Maehara A, Lansky AJ, de Bruyne B, Cristea E, Mintz GS, et al.; PROSPECT Investigators. A prospective natural-history study of coronary atherosclerosis. N Engl J Med. 2011;364(3):226-35. https://doi.org/10.1056/NEJMoa1002358. Erratum in: N Engl J Med. 2011;365(21):2040.
31. Waksman R, Di Mario C, Torguson R, Ali ZA, Singh V, Skinner WH, et al.; LRP Investigators. Identification of patients and plaques vulnerable to future coronary events with near-infrared spectroscopy intravascular ultrasound imaging: a prospective, cohort study. Lancet. 2019;394(10209):1629-37. https://doi.org/10.1016/S0140-6736(19)31794-5. Erratum in: Lancet. 2019;394(10209):1618.
32. Stone GW, Maehara A, Ali ZA, Held C, Matsumura M, Kjøller-Hansen L, et al.; PROSPECT ABSORB Investigators. Percutaneous coronary intervention for vulnerable coronary atherosclerotic plaque. J Am Coll Cardiol. 2020;76(20):2289-2301. https://doi.org/10.1016/j.jacc.2020.09.547
33. Seligman H, Shun-Shin MJ, Vasireddy A, Cook C, Ahmad YY, Howard J, et al. Fractional flow reserve derived from microcatheters versus standard pressure wires: a stenosis-level meta-analysis. Open Heart. 2019;6(1):e000971. https://doi.org/10.1136/openhrt-2018-000971. Erratum in: Open Heart. 2019;6(2):e000971corr1
34. Kawase Y, Omori H, Kawasaki M, Tanigaki T, Hirata T, Okamoto S, et al. Postocclusional hyperemia for fractional flow reserve after percutaneous coronary intervention. Circ Cardiovasc Interv. 2017;10(12):e005674. https://doi.org/10.1161/CIRCINTERVENTIONS.117.005674
35. Pontone G, Andreini D, Bartorelli AL, Bertella E, Cortinovis S, Mushtaq S, et al. A long-term prognostic value of CT angiography and exercise ECG in patients with suspected CAD. JACC Cardiovasc Imaging. 2013;6(6):641-50. https://doi.org/10.1016/j.jcmg.2013.01.015
36. Baggiano A, Fusini L, Del Torto A, Vivona P, Guglielmo M, Muscogiuri G, et al. Sequential strategy including FFRCT plus stress-CTP impacts on management of patients with stable chest pain: the stress-CTP RIPCORD Study. J Clin Med. 2020;9(7):2147. https://doi.org/10.3390/jcm9072147
37. Pontone G, Andreini D, Bartorelli AL, Cortinovis S, Mushtaq S, Bertella E, et al. Diagnostic accuracy of coronary computed tomography angiography: a comparison between prospective and retrospective electrocardiogram triggering. J Am Coll Cardiol. 2009;54(4):346-55. https://doi.org/10.1016/j.jacc.2009.04.027
38. Zech JR, Badgeley MA, Liu M, Costa AB, Titano JJ, Oermann EK. Variable generalization performance of a deep learning model to detect pneumonia in chest radiographs: A cross-sectional study. PLoS Med. 2018;15(11):e1002683. https://doi.org/10.1371/journal.pmed.1002683
39. Kim DW, Jang HY, Kim KW, Shin Y, Park SH. Design characteristics of studies reporting the performance of artificial intelligence algorithms for diagnostic analysis of medical images: results from recently published papers. Korean J Radiol. 2019;20(3):405-10.
40. Park SH, Han K. Methodologic guide for evaluating clinical performance and effect of artificial intelligence technology for medical diagnosis and prediction. Radiology. 2018;286(3):800-9.
41. Martin SS, van Assen M, Rapaka S, Hudson HT Jr, Fischer AM, Varga-Szemes A, et al. Evaluation of a deep learning-based automated CT coronary artery calcium scoring algorithm. JACC Cardiovasc Imaging. 2020;13(2 Pt 1):524-6. https://doi.org/10.1016/j.jcmg.2019.09.015 PMID:31734200
42. European Economic and Social Committee. White paper on artificial intelligence. 2020 [cited 2022 Sep. 6]. Available from: https://www.eesc.europa.eu/en/our-work/opinions-information-reports/opinions/white-paper-artificial-intelligence
43. Zuckerman DM, Brown P, Nissen SE. Medical device recalls and the FDA approval process. Arch Intern Med. 2011;171(11):1006-11. https://doi.org/10.1001/archinternmed.2011.30 PMID:21321283
44. Tat E, Bhatt DL, Rabbat MG. Addressing bias: artificial intelligence in cardiovascular medicine. Lancet Digit Health. 2020;2(12):e635-6. https://doi.org/10.1016/S2589-7500(20)30249-1
45. Geis JR, Brady AP, Wu CC, Spencer J, Ranschaert E, Jaremko JL, et al. Ethics of artificial intelligence in radiology: summary of the joint European and North American multisociety statement. J Am Coll Radiol. 2019;16(11):1516-21. https://doi.org/10.1016/j.jacr.2019.07.028 PMID:31585696

46. Muscogiuri G, Van Assen M, Tesche C, De Cecco CN, Chiesa M, Scafuri S, et al. Artificial intelligence in coronary computed tomography angiography: From anatomy to prognosis. Biomed Res Int. 2020;2020:6649410. doi: 10.1155/2020/6649410.
47. Itu L, Rapaka S, Passerini T, Georgescu B, Schwemmer C, Schoebinger M, et al. A machine-learning approach for computation of fractional flow reserve from coronary computed tomography. J Appl Physiol. 2016l;121(1):42-52. https://doi.org/10.1152/japplphysiol.00752.2015 PMID:27079692
48. Tang CX, Liu CY, Lu MJ, Schoepf UJ, Tesche C, Bayer RR 2nd, et al. CT FFR for ischemia-specific CAD with a new computational fluid dynamics algorithm: a Chinese multicenter study. JACC Cardiovasc Imaging. 2020;13(4):980-90. https://doi.org/10.1016/j.jcmg.2019.06.018 PMID:31422138
49. Xiong G, Kola D, Heo R, Elmore K, Cho I, Min JK. Myocardial perfusion analysis in cardiac computed tomography angiographic images at rest. Med Image Anal. 2015;24(1):77-89. https://doi.org/10.1016/j.media.2015.05.010 PMID:26073787