Coming up on Mayo Clinic Q&A,

Artificial intelligence is a form of very sophisticated pattern recognition. And through a process of repetition, maybe 100,000 times, where you show it an ECG, tell it what the right answer is, and it keeps tweaking it, it gets very, very good, and at the end, you have a math function.

That math function is an example of how artificial intelligence or AI is used in cardiovascular medicine. This enables for faster interpretation of the ECG, and...

if we do it right, it will detect diseases earlier, so that we can begin treatment sooner, and it will more equitably balance healthcare resources.
Welcome, everyone to Mayo Clinic Q&A. I’m Dr. Halena Gazelka. For many of us, we are living in an age of technology that we could only dream about decades ago. Things that we saw in cartoons or on television and in movies. When it comes to technology. Mayo Clinic is a leader in bringing the tools and science of artificial intelligence, or AI as it is known, to clinical practice. When it comes to the heart, Mayo Clinic’s artificial intelligence and cardiology work has looked at ways to use artificial intelligence both to predict and to diagnose heart diseases and conditions. Would you believe that there are even recent studies showing that artificial intelligence may be helpful in predicting COVID-19 infections? Well, here with us to discuss all of this today is Dr. Paul Friedman. Dr. Friedman is the chair of cardiovascular medicine at Mayo Clinic. Thanks for being here today, Paul. Welcome to the program.

Well, thank you. It’s a great pleasure to be with you.

I am so excited to discuss this topic with you because it absolutely amazes me.

Thank you.

I think it’s going to amaze our listeners too. I think one of the important things to understand, I know a lot of this work on artificial intelligence deals with electrocardiograms or ECGs. Would you explain for our listeners what those are?

Yeah, of course. So, the ECG or EKG, it’s the same thing, one is from Dutch one is English, is the recording of the heart’s electrical signals at a distance on the body’s surface. And typically, many of us have gone to the doctor you lay down, you get stickers on your chest, and those record the electrical signals, and we put them on a piece of paper. And it turns out that many of the diseases that affect the body will affect the electrical signals. Those electrical signals are governed by these tiny, microscopic channels that let currents go
through that are so critical to life, that they've evolved little from bacteria to human beings. Because if you think about it, every thought in your brain right now, every breath you take, every movement is controlled by electrical signals. And so, they're terribly important. It's not hard to believe that if there were a disease that were affecting heart muscle in any way that those electrical signals might be disrupted, and that it could potentially be an early finding.

Dr. Halena Gazelka 02:59
So, how does artificial intelligence apply to this?

Dr. Paul Friedman 03:01
Yeah, great question. So, right now, as clinicians, as you know, we're learning to read changes, for example, a segment or a named feature, ST segment elevation mean, someone may be having a heart attack, but there have to be millions of cells that are having problems for that change to happen. And artificial intelligence is a form of very sophisticated pattern recognition. And the way it works is you feed an ECG into what's called a neural network. And it's called that because it's modeled after human neurons, you have a number of math equations, they're all one connected to another, just like neurons are connected one to the other. And you feed in an ECG. And then for example, in the first network we built a screen for a weak heart pump, what we call a low ejection fraction. We would feed it an ECG and ask the network, is a weak heart pump present, and it would guess, it would have no idea. And then we train it. So, we say no, it may say ejection fraction 25%, we'd say no, this one's 45%. And then it changes the weights of all those equations just a little bit. And through a process of repetition, maybe 100,000 times where you show it an ECG, tell it with the right answer is and it keeps tweaking it, it gets very, very good. And at the end, you have a math function. And much the way you would show a child a fruit, and it's round and firm and has a stem, and you say apple, the children learns it is an apple, the computer learns the same thing, but instead of one or two examples, it needs hundreds of thousands or millions of examples. So, it takes a lot of computing to train the network, but once it's trained, you have a math equation you can run on a smartphone.

Dr. Halena Gazelka 04:39
So, it sounds like you've had to put many, many ECGs into the system with and without different diagnoses to make it accurate?
Dr. Paul Friedman 04:49
Yeah, that's exactly right. And one of the things we're really fortunate at Mayo Clinic is we have this huge digital data vault. And the people who came before me were very prescient, and we have a collection of just under 10 million digitally recorded ECGs sampled at roughly 500 hertz, and they're part of the electronic medical record. So, for any person's ECG, we also know what their blood test values are, what their echocardiographic or heart pump strength is. And so, we can use that to train the network because we need labeled data so that we can tell the network this ECG shows a normal heart pump, this one shows a weak heart pump. And what we've discovered is we started with heart pump strength, and we've gone on to identify a whole slew of conditions that affects the heart muscle, some are primary cardiac, some are not. So, we can develop a screening panel. And ECGs used to require you to lay down and put stickers on your chest. But as you know, you can now get it from a watch or a smartphone. So, it makes it a very powerful tool.

Dr. Halena Gazelka 05:52
Well, this sounds like this has come a long way from when I was back in medical school learning to measure little intervals on an EKG with a caliper and they always said don't believe the machine and what it read. You have to read the ECG yourself. Do you remember those days?

Dr. Paul Friedman 06:06
I definitely do. I definitely do. Increasingly, we need to learn to believe the machine, although as always, it's a tool, and we use it with judgment. And, you know, people say is AI, speaking broadly, going to replace us? Will it do everything we do? And the way I look at it is this, if you want to go for a walk on a dark night, you're going to take a flashlight. And with a flashlight, you'll be able to see, but the flashlight is empowering your eyes, it's not replacing them. And so, these are powerful tools that will let us see deeper and farther into the future.

Dr. Halena Gazelka 06:40
That's great. Tell me how is this useful in clinical practice? How do we know we can rely on it?

Dr. Paul Friedman 06:45
Yeah, great question. So, we started like any tool that has to be vetted and validated and confirmed. And so, we are in the process, and have done a number of studies to show just that. So, for example, for the weak heart pump ECG, we've put it into our dashboard, so it's available within the Mayo Clinic system, as you know, in any patient, when we look at their record, we can see all ECGs now. And we did a prospective trial with roughly 120 primary care practices. So, these were busy clinicians taking care of patients and clinics on the front line, no expertise in artificial intelligence, and we randomized the clinics, not the patients. So, half of the clinics got the results of the AI. So, they would order an ECG because clinically it was necessary. They're seeing a patient, say I need an electrocardiogram, they order it, and they get the report, and it says, by the way, I suspect a low ejection fraction. They were told they would get that information, and then they could do what they wanted with it. The other half didn't get that information. And what we found was that when you have that information available, you become a better clinician, you're more likely to identify the presence of a weak heart pump, because now you have a clue that it's there. And interestingly, it didn't increase the overall utilization of echocardiograms, the imaging tests we do to confirm a weak heart pump, but rather made us better at picking who to order them on.

Dr. Halena Gazelka 08:12
Isn't that interesting? Is it also being used then to predict whether someone will go into heart failure?

Dr. Paul Friedman 08:19
Great question.

Dr. Halena Gazelka 08:20
Hospitalization is a concern for these patients.

Dr. Paul Friedman 08:22
Yeah. So, you know when we first did this, we measured the power of these tests with what's called the AUC, or area under the curve. And so, you know, like a pap smear has a value of 0.7 and we want it to be a perfect test. A treadmill test is 0.85. This test, the computer's ability to read your ECG and say, hey, you have a weak heart pump is 0.93, really powerful. But to get to your question, what was really striking was when it gave us what we thought was a false positive. So, ECG goes into the computer, computer says, weak heart pump, you then do the gold standard test, the echocardiogram, the
ultrasound of the heart, and it says, no, it’s normal, you got it wrong. You then look at that person five years down the road, they have a five-fold increased risk of developing a weak heart pump. So, it seems like magic, like it’s predicting the future. But what’s actually happening is, there’s a pathologic process that’s affecting all those ion channels. And before the heart muscle’s ability to contract is affected, the electrical signals are very subtly disrupted. And unlike the heart attack that you and I can look at an ECG and go, oh, you know, there’s a lot of cells, here they’re subtle, they’re likely nonlinear. They’re affecting multiple small features, so that humans aren’t trained in how to you know, find these things. And most of us, even those of us who have spent a lot of time looking at ECGs, look at it and go, I’m not sure I see a problem here, and the computer spits it out. And you follow that person for a few years, and it predicts a problem. And so, the predictive power is actually a striking finding seen across multiple disease states. And that’s actually maybe one of its potentially great uses knowing who to screen for a weak heart pump, or a condition called amyloid heart disease, which it can pick up maybe a year before you’d otherwise know about it. So, you can potentially start treatment sooner.

Dr. Halena Gazelka  10:12
That is so fascinating to me, Paul. It reminds me of a snowflake, and how you always learned in elementary school that no two snowflakes are alike. And it got me to wondering if these are so precise, can you tell an individual, identify an individual with their EKG? That might not be something that we know yet, but it’s a curiosity.

Dr. Paul Friedman  10:32
Actually, you can. It’s not something we’ve done. But there have been published reports that like a fingerprint, an ECG can be an individual identifier. And so, it was really interesting. When we initially developed the weak heart pump ECG, we just fed the computer the ECG. Essentially, voltage recorded from your skin over time, we didn’t say, Are you a man or a woman? How old is the person? But we know heart disease is impacted by your age and your gender. So, we then added those features to the model, to the computer, we said, by the way, the person whose ECG is x years old, and is a man or a woman and whatnot. And to our amazement, it had no improvement at all. It made no impact. And then we thought maybe the computer already knows whether you’re a man or a woman from reading your ECG. So, we asked it. We trained a network and asked it. The ability for a computer to read your ECG and tell whether you are a man or woman, the area under the curve is 0.97, almost perfect. In other words, the computer reading someone’s ECG is better at determining whether that person is a man or a woman than you or I walking down the street looking at that person. I mean, it’s really remarkable,
Dr. Halena Gazelka 11:45
That is truly fascinating. That kind of leads to my next question, then, which is, when you’re having to use all of this data to perfect these algorithms, how do you protect personal patient data?

Dr. Paul Friedman 11:57
Yeah, that's a great question. And as you're aware, Mayo Clinic takes data privacy very, very seriously. It’s at the root of our mission really in protecting patients. And there are a couple of measures in place. The first is that data when they’re used for research, they’re de identified, we don’t have individual’s names. The second is anyone whose data we use has given consent for data usage, it’s part of the standard when people come, they give permission for their data to be used in a non-identifiable way. And then there are ongoing conferences and committees that look at data protection to ensure we’re always doing our best to do that. And of course, each of these are done under the setting of an IRB review. So, an institutional review board if people who are not part of the study are looking at it to ensure patients are protected, as with any research.

Dr. Halena Gazelka 12:48
And, Paul, you just talked about a little bit ago about how much data it takes to make one of these algorithms. Do you anticipate that as we have more and more data that the algorithms will continue to change? Or will we stop at something?

Dr. Paul Friedman 13:03
No, I mean a really good question on multiple levels. The first one is data from different people with different backgrounds, genetic backgrounds, different ethnicities, and races. And we want to make sure that if we build a test, that it’s widely usable, and adaptable. So, one of the things we’ve done is tested it on diverse populations within our own hospitals, and then at other hospitals, we’ve collaborated and to confirm, and hospitals, in Korea, in Africa, in Russia, in European countries, does it still work. And this particular algorithm does. But you can’t make that assumption. There have been cases where artificial intelligence that works, for example, facial recognition, has worked well in one race and not in another race. And that’s a big problem, for example, for using that in law enforcement or other things. And so, you know, we have to be very careful, again, as with any medical tests, that we train it on a broad network, because the networks are very powerful in identifying patterns they’ve seen. But if there’s a difference because of genetic or racial differences in an ECG, and in fact, there are, and so when we did do a study
looking for bias, the network works across all races, but it can also identify race based on an ECG.

Dr. Halena Gazelka 14:27
Fascinating. So, that’s a lot that you’re working on. What of the cardiac algorithms do you see being most practical in clinical practice? And how would you apply them?

Dr. Paul Friedman 14:39
Yeah, so there are a couple of areas where I think they’ll be very helpful. The, first one is, anytime you get an ECG, we get a lot of inflammation as it is, but there’s a lot we’re learning we can screen for. And right now, today, there’s probably at least a half dozen, probably more, closer to 10 tests that are tested and published. And some are in the process of regulatory approval, so that your standard history and physical can also screen for disease that is occult, that might otherwise not be detected. And the hope is that we then better utilize healthcare resources. So, we send people who need to go for imaging for echocardiograms, or CT scans, who will benefit from it. And if everything looks okay, we don’t put you through that extra test and expense and exposure to radiation or whatever else is involved. So, I see that happening within a year, you know, in terms of widely available in ECGs. As you know, we have them as clinical guidance in our own practice now, but we need regulatory approval and the collection of all these data to make them widely available. And ultimately, you know, as part of the Mayo Clinic platform, where we try to make health information widely available across the country and globally, you know, that’s the vision that this becomes part of and supports the Mayo Clinic larger platform vision. And then there will be portable versions, you know, using mobile phones, smartwatches devices like these, that connect to a smart, you know, these little electrodes that connect to your smartphone. And, you know, we recently saw, for example, a Danish soccer player go down in the field, which was, you know, striking and upsetting, and to see a healthy young athlete in his prime collapse, and fortunately, he was resuscitated, and he’s not doing well. But many of these conditions can be detected if we had powerful enough screening tools. One of the tools that we have published on for example, screens for a thickened heart muscle called hypertrophic cardiomyopathy, very uncommon, but if present can lead to collapse. So, you know, I do think that these may impact screening, there may be a role in screening pregnant women for this very uncommon condition that can happen of a weak heart pump. So, we have a number of trials that are sort of underway looking at these things.

Dr. Halena Gazelka 16:57
So, Paul that makes me curious, when we talked about how much data is needed to be able to perfect these algorithms, how are they useful, and how do you get enough information in conditions that are a bit more rare?

Dr. Paul Friedman 17:10
That’s really difficult. And, you know, we’re fortunate in our own data set that we have, even in rare conditions in our referral practice, we have a fair number. So, we have 1000s, small 1000s of patients with hypertrophic cardiomyopathy enough so that we could use those to train a network. And ultimately, you do have to have a minimum number to teach the network because they are slow learners in a way, right. You need exposure and exposure for the network to keep adjusting its math function to get it just right and to be useful. There are some tools being developed that may allow network development with a smaller number of samples, but those aren’t really robust yet. And that’s more sort of AI research, computer science research work. Paul, what you said earlier about Apple Watches got me intrigued. I have my Apple watch on, and of course I have my phone and I can look at my ECG tracing on it. Will I be able to send that to you, my cardiologist, someday to look at that and interpret it for me? The short answer is, yes. Right now, you can do it by email. But it’s a real problem. I had a patient, you know, a week or two ago who brought in a folder of printed Apple Watch printouts, and it was useful, it actually helped make the diagnosis. But it’s ironic, right? It’s a digital thing. She comes from miles, she could have sent it electronically. But she brought the folder, and we went through it together, and it was very helpful. We will be starting a study where any person who has the Mayo Clinic app can automatically in a secure manner, send their Apple Watch ECGs, and they’ll go into our electronic medical record. So, if you think about what that means, you don’t have to email it, which is not secure. You don’t have to send it to me directly. So, if I’m on vacation, one of my colleagues can see it because it’s in the record. And the goal will be just to show that they’re clinically useful. And I think they will be often, but we’ll define that better. That will be the standard ECG. Once we have a lot of those. The next question, of course, will be, can we use these AI tools to identify things that normally you couldn’t see that a human reader can’t see from an ECG, like a weak heart pump, or like the presence of silent arrhythmia from an Apple Watch recording or from an other smartphone recording? And I think, you know, that’s something and this is a project that is being done in collaboration with Mayo Clinic Center for Digital health. They’ve done a phenomenal job and have the resources to create a user-friendly app, which they’ve done to test this hypothesis. And then if it works out, I imagine it would become part of the Mayo Clinic app, so anyone with a Mayo Clinic app, no matter where you are, could send ECGs, and your Mayo Clinic provider would be able to look at them.
Dr. Halena Gazelka 19:57
That is just fascinating. It's amazing hearing the things that are going on that we could only imagine.

Dr. Paul Friedman 20:03
It is remarkable.

Dr. Halena Gazelka 20:04
Paul, I want to turn to a couple of questions about COVID and AI. What in the world does COVID have to do with an ECG anyway?

Dr. Paul Friedman 20:14
That's a great question. And you know, when COVID first came, all of us were scrambling, how can we help? What can we do? And a colleague of mine Dr. Suraj Kapa, sent me this article from 1999 of Coronavirus infection and rabbits, changing the ECG. And I thought that's interesting. And many of the changes were subtle and nonspecific. But of course, that's what neural networks excel at. And then we saw the early reports out of Wuhan showing that people who were getting infected with COVID, were having heart problems. And these are troponins, so a chemical released by heart muscles in the bloodstream. And the SARS-CoV-2 virus binds to cells using a spike protein on the virus that binds to an H2 receptor. So, this receptor is sort of a lock and key mechanism. And that receptor, of course, is all over the lungs, which is why people get cough and lung infection. But it turns out, it's widely expressed in the heart. So, we thought, you know, if we know that they're in an animal model there are ECG changes, and we know the virus binds to this receptor that's in the heart, maybe we'll see ECG changes, ideally early in the disease, but we don't really know when, and that those could be used as a screen. I mean, the vision was, you want to get on an airplane, you put your hands on electrodes for 15 seconds. And if it's okay, you know, you're good to go. So, we contacted hospitals, literally from around the world, on four continents, and in more than 20 countries. And keep in mind, this is in the middle of a horrendous pandemic, hospitals are swamped. Doctors, nurses, administrators, everyone's overwhelmed. And people just stepped up to the plate. And all said we want to help, we're glad to do it. We learned a lot about the complexities of getting digital data transmitted from around the world, it's not straightforward. We had a volunteer partnership from industry also to facilitate that. And we collected over 40,000 ECGs. And with those, we had some from people who we knew had COVID, they had a positive PCR test. And then we had some that we knew didn't have COVID, because it was either a certain period of time before their infection, or we took ECGs, from before
October of 2019, when COVID didn't exist. And what we found was that with this network, you can in fact, detect COVID infection. So, the negative predictive value, so if you assume like 5% of the people in an area have COVID, if you have an ECG that says you don't have COVID, then the negative predictive value is 99%. So, a pretty powerful test. Now, there's some caveats here. This was retrospective, we haven't completed a prospective study which was started as a consequence of that. We don't know how sick you have to be along the spectrum to get these ECG changes. And we haven't confirmed whether it's COVID specifically, or the degree of illness. And so, I think, again as with any tests, we have to vet and validate and confirm, before we can use it in the screening model we hope for. Then that remains to be determined. But certainly, the signal is there, that COVID infection causes ECG changes.

Dr. Halena Gazelka 23:28
So Paul, let me just be sure that I understand this. So, when we first started testing for COVID, we were doing nasal swabs, taking days to get results back. Now we are swabbing and able to get results back almost instantaneously with some of the tests. In fact, I saw testing centers in the airport, when I was last in the Minneapolis airport. And this would be using a cardiac rhythm, so completely non-invasive.

Dr. Paul Friedman 23:54
Right.

Dr. Halena Gazelka 23:54
And you'd read it, the algorithm would then hopefully, if it works, read it in the moment and be able to tell if somebody might have COVID.

Dr. Paul Friedman 24:02
So, the way we work, is you put your hands on the electrodes. And again, we tested 12 leads, and many of our other algorithms have worked when we've reduced it from a 12 lead on your chest, to on your hands. But we don't know about this one yet. So, it would be on your hands, and if it works, it would be for 30 seconds, or 15 seconds, and then it would tell you right away. It would either say you don't have COVID get on the airplane, or it would say not sure, better get the swab. But it would cut down on swabs, maybe cut down on time. So, an interesting signal that requires further exploration.
Dr. Halena Gazelka 24:38
Well, you mentioned earlier that when you’re doing this type of research, you were trying to get information from around the world. We have a lot of patients and a lot of testing centers in the United States. Why would it be important to involve individuals from all around the world, their data when you’re building algorithms?

Dr. Paul Friedman 24:57
Yeah, great, great point. So first, we do involve people from around the US and around the world. So, it’s not just us and you know, other countries. But the reasons there are a couple. First for COVID, because there were different hotspots at different times, and it was, you know, more useful to get data from hotspots. Then in general, for neural networks, we want to be sure they’re widely applicable. We want to make sure that the network isn’t trained, for example, only on Caucasian people, and then if we were to use it on, say, someone of Asian descent or an African American, that it hadn’t seen the subtle differences that may be genetically encoded in the ECG, and not get as accurate of an answer. So, we really want to be mindful. And it’s true, really, of all neural networks, a very patterned, you know, a specific learning. It’s the same thing with driving cars, if you train it on the interstate, they may do a great job there, but you put it on a city street, if it’s never seen a red light, it’ll ignore it most likely. And so, you know, same thing here, we want to make sure that they’re widely generalizable.

Dr. Halena Gazelka 24:57
I was thinking about the fact that, you know, we’re always concerned that we want to be certain that testing obviously, is very accurate. And I remember the days, I sound so old when I say these things, that a lot of the cardiac testing and data that came out was on males, much more than females. And of course, that’s been rectified. But also, it’s obviously important not to have disparities in terms of race when you’re doing studies as well.

Dr. Paul Friedman 26:24
That’s very true. And you make a really good point about cardiac studies. And I would say it’s been maybe incompletely rectified, there’s still a gap in our data set. It’s easiest to assess for sex, where there is a clear discrepancy. But it also exists with race as well. And I think there is keen interest and a lot of effort on the part of many institutions, including now, to make sure that we represent all of humanity in what we learn so that we can care for all of humanity and care for each other irrespective of sex, of ethnicity of race, or any
other factors.

Dr. Halena Gazelka 27:02
Paul, this is all very exciting. And it almost sounds like the sky is the limit. What do you see down the road for artificial intelligence and cardiovascular research?

Dr. Paul Friedman 27:12
Yeah. So, it is very exciting. At the same time, I think we have to be very diligent and how we test that invalidate. But you know, for at least for some of these tests, that's being done, and it's looking very promising. And so, you know, what I think happening is, it will push everyone to the top of his or her license. And I suspect that primary care, for example, will be more involved, at least in the initial diagnosis of heart disease, I think that's a good thing. There's too much heart disease to have everyone referred. And my hope is that if we apply this properly, it will better utilize resources. And so, you and I will be seeing the kinds of people who we spent a lot of time training to get really good at sub, sub specialty problems. And those people who don't need that kind of attention and care and training and expertise, won't need to make the trip to come see us. And that'll give more capacity for the kinds of things so if we do it right, it will detect diseases earlier, so that we can begin treatment sooner, and it will more equitably balance health care resources. And know I'm an optimist, but I'm also a realist. And I recognize the amount of work and commitment to effort it takes to get to that point.

Dr. Halena Gazelka 28:28
And what is amazing is we're talking about cardiology today, but AI is being applied in many areas of medicine, I've heard some of our radiologists talking about using chest x-rays, for instance, and their predictive value. So, there's a lot more to this.

Dr. Paul Friedman 28:42
I think it'll be huge. And it will just empower all the tools that all of us use. You know, I can see you would have a lot of immediate use in neurology, gastroenterology. I suspect it'll impact anesthesiology as well in a whole slew of ways. So, I do think as we're thoughtful about developing our tools, and as clinicians, our role, I think, is to learn what AI can and can't do. And as you know, there are a lot of efforts now to modify or add to our training of physicians, so they know how to use these tools, so that we can both develop new tools and make them widely available.
Dr. Halena Gazelka 29:20
I’m going to have to become more tech savvy huh Paul?

Dr. Paul Friedman 29:24
Actually, you know, that’s an interesting point. I think our clinical expertise is what’s critical to train the AI. And I think it’s more a matter of partnering with our engineers. I work very closely with an AI scientist, Dr. Zachi Attia, who has driven a lot of these. And we both learn a lot from each other. I learned a whole new language about AI. And he’s come in and watched me do procedures, for example, and a lot of the ideas come out of that. He’ll ask a simple question like, well why did you do that? And my answer is, well, that’s how I was trained to do it. And he’ll go but why? And then we’ll start thinking about it, and that’s how you come up with new ideas. Why are we doing it that way? And as you know, many things have evolved over time and it’s that kind of going back to first principles that really drives new ideas.

Dr. Halena Gazelka 30:05
Just fascinating. Thanks for being here today, Paul,

Dr. Paul Friedman 30:08
Thank you so much. It’s been fun.

Dr. Halena Gazelka 30:10
Our thanks to Mayo Clinic cardiologist, Dr. Paul Friedman, for being here today to talk to us about artificial intelligence in cardiology. I hope that you learned something. I know that I did. We wish each of you a wonderful day.

Narrator 30:23
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