Transcript What is ECG Age Vs. Chronological Age

Dr. Stephen Kopecky: Hello, I'm Dr. Steve Kopecky, preventive cardiologist at Mayo Clinic in Rochester, Minnesota. And this is one of the continuing series of interviews with the experts in pr, cardiovascular disease prevention. Today I'm delighted to introduce Dr. Francisco Lopez-Jimenez who is a friend and colleague. He's chair of our cardiovascular disease prevention section called Cardiovascular Health Clinic, and has done some amazing work with some of our cardiology colleagues on ECG age as defined by the electrocardiogram and versus chronologic age. So welcome Francisco.

Dr. Francisco Lopez-Jimenez: Thank you, Steve. It is an honor and a pleasure to be here. Thank you for the invitation.

- Dr. Stephen Kopecky: Well, the work you y'all have done is just fantastic. And, and tell us simply what is ECG age?

Dr. Francisco Lopez-Jimenez: Well, ECG age is a concept that refers to an estimated age that is derived from analyzing patient's electrocardiograms using artificial intelligence or more specifically machine learning. So basically the computer is trained to guess the person's age, and after being trained to guess the age, the, the result is gonna be a number that might be exactly the same as the chronological age. Might be older, might be younger. And we believe that these ECG age reflects the biological age. That is not necessarily the same as the chronological age as we know it.

Dr. Stephen Kopecky: There's just so much data in an ECG, there must be that you can correlate this. How did you come up with this idea?

Dr. Francisco Lopez-Jimenez: Well, you know, as interesting and as cool this concept is, the truth is that we found it by serendipity, we were not planning on this. The study is that as we were working on a different algorithm, trying to predict low left ventricular ejection fraction or low pumping function of the heart, we tested the, the additional value that putting sex and age into the model will improve the prediction of this condition. And to our surprise, adding age and sex did not improve the performance of the model at all. Nothing, absolutely nothing. And biostatisticians know that when that happens in a model, it's either that those variables don't matter, or if they do matter to predict something and the model doesn't change, what that means is that very likely the computer already knows age and sex. So from there, one of our, I mean our lead engineer back then, Dr. Itzhak Zachi Attia, he tested the hypothesis that indeed the computer can predict age and sex. And sure enough, we saw that using artificial intelligence, we can train the computer to predict age. And that was basically the, the, the origin of that. The, the next step was to essentially see the, the value of that, the meaning of that. Because even though we saw that the computer was able to predict age,

the prediction was not perfect. So the question was, is that imperfection related to just error, the inability of the computer to predict age or is that telling us something else? And from that point, we did a series of studies trying to prove the principle that, or the, the hypothesis or concept that ECG age was indeed measuring biological age or in other words, the, the, the speed at which the person has been aging. Meaning that if the prediction was a higher age, that person has been aging faster, and if the predicted age was lower, that person has been aging slower than, than normal.

Dr. Stephen Kopecky: Why do you think it's important to know biological age versus chronological age? How do you use that?

Dr. Francisco Lopez-Jimenez: See, the, the concept of biological age is not new. I think it's important to clarify, we did not invent that we invented the, the, the principle to measure or to calculate age using the electrocardiogram with artificial intelligence. But the concept of biological age has been around for many decades. And it's important because biologists at some point found out that not everybody ages at the same rate, or equally, you know, aging is a, is a, is a process that essentially reflects the, the exposure of our cells, our organs, our systems to many factors, many factors that affect their function, their integrity. And as we get older, the body loses the ability to regenerate itself or the cells and the organs. And that is essentially the concept of aging. Now, biological aging will be the rate at which that aging occurs. That if biological aging is fast, it, it might actually reflect either undiagnosed disease conditions, it might reflect some genetic predisposition to, to age faster. It might reflect effect of stressors or external factors in the environment that might be triggering a faster aging. So, so we believe this is an extremely important biomarker in many ways, although we are still trying to find what is the best place of this biomarker in clinical medicine.

Dr. Stephen Kopecky: So there are obviously many things that can affect it, how you eat your stress, your sleep, et cetera, your genes. What about things that, what does it predict? Is it, can you give us any specifics? Does it prevent a heart attack or predict a stroke? Does it predict cardiovascular death or just too many, too many things to, to mention?

Dr. Francisco Lopez-Jimenez: Yeah, no, that's an, that's a, an excellent question. But before I answer that, let me first state the, the things that we have found to affect biological age, and then I will tell you a little bit on, on what the biological age can then predict. We have found that, for example, having genes that are known to cause some very rare conditions where the person ages very fast. You know, things like progeria where people age twice or three times or four times faster than normal, that individuals that are the age of 30, they actually look literally like if they were 60 or 70 or 80. Okay. So those genes definitely affect this. And patients with those genes present are about 21 years older biologically compared to control. So that's one. But we have found that, you know, standard things from factors that we are exposed in a daily basis can also affect this. For example, high stress appears to make people age faster, lack of exercise as well. Having a high cholesterol also correlates with biological age. We have found that social isolation and many social

determinants of health correlate with a, a accelerated biological age. Now nothing really comes as a surprise, but it's very interesting that all those things that relate to heart disease and and many other disease conditions also relate to biological aging. Now, biological aging has shown to predict survival. For example, those with a, with a higher biological age using the ECG die sooner compared to those where the age that is calculated by the ECG is very similar to the chronological age. And by the other hand, those that appear to be younger biologically actually live longer. This also predicts rates of heart attacks, myocardial infarction, and also stroke. We have shown that advanced biological age correlates with subclinical coronary disease measured with coronary calcium in the heart. We have shown that biological age also predicts like many other effects in, in individuals. For example, a kidney transplant recipient candidates, those that are waiting for a to be to to receive the transplant. Individuals with a, with a higher biological age actually do worse during the transplant. And the list goes on and on. But essentially things that we know relate to age in general are very likely related to rapid aging or an advanced biological age.

Dr. Stephen Kopecky: That's, that's fantastic. You know, I, I use this frequently in my practice here in prevention and point out to patients that this can change in just a few months, you know, change how they eat, change how they exercise, change their stress levels, their sleep. Is that, have you found that in your, in your studies?

Dr. Francisco Lopez-Jimenez: Absolutely. And, and, and, and, and like you, I use this also as a teaching point to show my patients that even though they might feel good, they might feel very healthy, even though pretty much everything else we test on them might show to be completely normal. But individuals who are not exercising regularly, who are very sedentary, smoking a lot, and also not taking care of themselves in many ways, oftentimes the biological age chose to be higher or much higher than, than their chronological age. And I use that to essentially show them that they are very likely aging much faster than they should. So we use that all the time and, and we believe that the potential is probably even greater, that we still have, haven't untapped the whole potential.

Dr. Stephen Kopecky: Hmm. Have you studied this to see how it motivates patients to change lifestyle, adhere to meds, et cetera?

Dr. Francisco Lopez-Jimenez: Excellent question. We haven't, and I, and I think that will be a, a, a fascinating study now. So something that, you know, one of the most recent studies we have done that was fascinating and, and the hypothesis came because one of my colleagues who is, is, is now a, a a a, an investigator at Mayo Clinic, but used to be a, a postdoc fellow. And, and this person came to me very concerned because she had been doing some ECGs for, for a couple of years. And at the beginning she was very happy because ECG will say that she was like a 10 or 15 years younger than her current real age. But it occurred that at one point she actually became older by ECG out of blue and then a subsequent electrocardiogram show again that she was again younger than than normal. So she was puzzle like I was that an error, you know, how can we explain that?

Because she was mortified by that change. So I asked her, so, so what were you doing around those those days? I mean, is there anything important in your life? And sure enough, those were the days when she actually had to defend her thesis, her PhD thesis. So, so basically that triggered a hypothesis that, well, stress, acute stress might affect the aging process significantly. And we know that stress is bad, right? But it was fascinating to see this now in the most recent experiment triggered by that incident, creating the hypothesis that acute stress might even temporarily make people older. We tested in a, in a beautiful experiment known by some colleagues from from Emory that they got ECGs, a baseline ECGs during experimental mental stress. They were causing on, on studies objects and then ECGs afterwards, and guess what happened to the ECG age? ECG age went up during the acute stress and went down to baseline. Something very interesting is that people responded in different ways. Some people barely had any change, others didn't change at all. In others, there was an increase in, in, in biological age, and some people the age went to the roof during that mental stress. Another very interesting concept for us to do more research on,

Dr. Stephen Kopecky: Certainly, well, we've known for years that stress will increase, cholesterol levels, will increase blood pressure. I'm sure that's all interrelated.

Dr. Francisco Lopez-Jimenez: Exactly.

Dr. Stephen Kopecky: Francisco, how finally, how, how do you get this, I mean, you'd get it from a 12 lead ECG, but how can, can people, physicians around the country, patients around the country get access?

Dr. Francisco Lopez-Jimenez: Yeah, well, you know, unfortunately the implementation of ai, ECG hasn't been very good, to be very honest. There are a lot of steps that need to occur before those algorithms can be implemented. First of all, algorithms that are meant to detect disease conditions have to go through very strict regulatory approval process by the FDA, which I think is, is good to have that process, but, but it's, take it, it really takes a long time. Now algorithms like this that might not need to go through that regulatory process still require medical centers to have the algorithms available, to have the system in place where the electrocardiograms are processed, not just through the regular computer processing to, to get preliminary diagnosis as, as we have been doing for 30 years, but also to do the AI analysis to determine many things. One of those could be biological age. We hope this, this will change in the, in the, in the near future. So everybody can check this out and, and ideally will be actually that people can check their biological age, not only with the full electrocardiogram, but also using some point of care devices that people can just put their fingers on or smart watches or cell phones.

Dr. Stephen Kopecky: Well, this has been a fan-fascinating discussion, Francisco, thank you for talking to us about chronologic age versus biologic age as assessed by the 12 lead, ECG. This is

certainly something that, you know, we're using in our practice here. I think it's fascinating that it changes quickly with a poor lifestyle, improves with, you know, with a good lifestyle. And I think we'll be hearing much more about this in the future. And thank you for your leadership in this and for educating us all today.

Dr. Francisco Lopez-Jimenez: Well, thank you for the invitation.