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Mayo Clinic researchers use AI and genetics to identify early signs of a rare, life-threatening heart condition

Susan Murphy

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ROCHESTER, Minn. — At Mayo Clinic, cardiologists Peter Noseworthy, M.D., and John Giudicessi, M.D., Ph.D., are uncovering the earliest signs of a genetic heart condition that often strikes without warning. Their work shows that early detection, and even prevention, may be

possible long before symptoms appear.

The condition, arrhythmogenic right ventricular cardiomyopathy, weakens the molecules that hold heart cells together. As those bonds deteriorate, healthy muscle is replaced with scar tissue and fat, leaving the heart weaker.

The disease often advances silently. Sometimes the first sign is when a person suddenly collapses during exercise. For many, a diagnosis comes only after the heart is already damaged. Detecting it earlier could spare patients from heart failure, the need for a transplant or sudden death.

Dr. Peter Noseworthy

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"We spend so much time managing the consequences of this disease — ablations, transplants, repeated hospitalizations," Dr. Noseworthy says. "It's a much better paradigm to ask: What can we do to prevent this in the first place?"

Leading a new era of heart care

Dr. Noseworthy leads Mayo Clinic's Division of Heart Rhythm Services, where he cares for patients with heart rhythm disorders and helps guide innovation strategies across the institution. Much of his research centers on using digital tools and artificial intelligence (AI) to detect problems earlier and improve patient care.

Dr. Giudicessi, a genetic cardiologist, focuses on inherited heart rhythm conditions and how genetic changes influence who develops disease. His work bridges patient care and laboratory research, including first-in-human clinical trials that explore the potential of gene therapy.

Together, they turned to two powerful data sources: the genetic code that shapes the heart and the electrical signals that guide its rhythm.

Dr. John Giudicessi

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Pinpointing risk in genes and rhythm

Their search for answers started in Mayo Clinic's new Research Data Atlas, which unites decades of genetic, clinical and biospecimen data. Within it, they identified people carrying disease-causing mutations in PKP2, the gene most often linked to this disease.

About 1 in 2,000 people carry a mutation in the PKP2 gene, but many never develop the disease. The challenge is knowing who will — and stepping in early enough to change the outcome. That question drives Dr. Giudicessi's work.

"So much of medicine is reactionary — we wait for something bad to happen," Dr. Giudicessi says. "This work is ushering in the tools to push against disease and to identify it early."

To spot those early rhythm changes, the team drew on an AI model developed by Mayo Clinic cardiologist Ammar Killu, M.B.B.S., and his team.

Analyzing electrocardiograms from patients with a PKP2 mutation, the AI helped the researchers identify faint patterns that marked the first signs of disease.

Dr. Ammar Killu

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"This research shows how AI can help us identify really subtle changes that may facilitate earlier diagnosis and then allow us to move beyond individual cases to understand patterns across populations," Dr. Killu says. "It's a powerful example of how we can scale early detection to reach more patients before disease takes hold."

Those insights led to a next step. Guided by the AI findings, Dr. Noseworthy and Dr. Giudicessi provided smartwatches to people who were showing early signs of disease. The devices help track daily activity levels — important data, since strenuous exercise can accelerate the disease, while even small adjustments may help slow it.

The researchers are also exploring gene therapy for PKP2. Still in early testing, the approach may one day restore the missing gene and keep the disease from advancing.

Building medicine's next chapter

Their work is part of a larger shift at Mayo Clinic: predicting and preventing disease before it takes hold. That vision drives Precure, an initiative to intercept serious conditions early enough to alter their course. With tools like the Research Data Atlas, investigators can study health patterns across large populations, detect risk sooner and potentially guide people to care before disease advances.

For Dr. Noseworthy, Dr. Giudicessi and Dr. Killu, the vision is bigger than a single study. They are helping build the infrastructure to move medicine earlier in the course of disease, where illness can be intercepted at scale.

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Media contact:

- Terri Malloy, Mayo Clinic Communications, newsbureau@mayo.edu