Sanjiv Shah is a cardiologist at Northwestern Memorial Hospital and an associate professor at the Feinberg School of Medicine. He specializes in echocardiography and heart failure, a syndrome with several pathophysiologic contributors leading to the inability of the heart to keep up to the demands of the body.

There are two main types of heart failure: reduced ejection fraction (HFrEF, also known as systolic heart failure) and preserved ejection fraction (HFpEF, known as diastolic heart failure). In the former instance, the heart pumps too little oxygen-rich blood; in the latter, the muscle contracts normally but its ventricles do not properly relax, which can result in fluid retention in the lungs and the body, leading to congestive heart failure.

“The prevalence of HFpEF is increasing, with more than 3 million Americans currently afflicted,” says Shah, who is director of the Northwestern HFpEF Program as well as director for the University’s T1 Center for Developmental Cardiovascular Therapeutics. Today, about 50 percent of all heart failure patients have preserved EF; and this proportion and overall prevalence has been increasing over time, he notes. Once hospitalized with HFpEF, the 5-year survival rate is poor: just 35 percent.

Yet despite these numbers, clinical trial enrollment has proven challenging: Globally across six countries and 270 sites, only 2.6 patients per site were enrolled each year in TOpCAT, a large HFpEF clinical trial. Northwestern’s HFpEF program is a distinguished exception, enrolling 77 patients in the TOPCAT trial.

Northwestern’s HFpEF Program, started by Shah in 2007, is the first and largest dedicated HFpEF program in the world, having cared for more than 1,500 patients with HFpEF, results in part attributable to innovative data analysis to identify these patients.

While the management of systolic heart failure has improved over the past 30 years, finding effective treatments and conducting clinical trials for HFpEF globally have proven more challenging. There is currently no diagnostic test for the condition. Because general practitioners, geriatricians, pulmonologists, as well as cardiologists, often care for HFpEF patients, this further complicates identifying trial candidates. Shah also says the condition’s lack of targeted therapies sometimes results in “therapeutic nihilism,” where clinicians feel that there are no viable treatments and so are less likely to refer patients to specialists or for trials—especially if they perceive competing health risks for the patient.

Dr. Shah earned his MD from Northwestern’s Feinberg School in 2000, where he was an HPME student. He completed his medical residency at the University of California-San Francisco (UCSF) in 2003 and a cardiology fellowship at UCSF in 2006. Research News recently spoke with Shah about his medical research and some of the experiences informing it.

What was your earliest research project?
In the 7th grade I was an avid tennis player, so I tried to determine the relative efficacy of several vibration dampeners (shock absorbers) for tennis rackets. For a science fair, I devised a contraption in my basement that consisted of a tennis racket handle secured to a foot pump, which I used to fill my bike tires. The pump was on a spring-loaded mechanism. I had a tennis ball hanging by a string from the ceiling and I studied the various trajectories that occurred when the racket hit the ball.

This study’s second part consisted of a pen secured to the racket’s head with the tip of the pen continuously marking a roll of cash register paper as it spun on a tape recorder mechanism. As the ball hit the racket, the “shock pattern” would be recorded on the paper, and I analyzed the differential shock patterns coming from the racket with each type of shock absorber.

Sounds quite inventive. How did you do in the science fair?
I came in second place to a descriptive project explaining how wood pulp is turned into paper. I still remember the tough loss, but I emerged determined to fight harder next time. That drive to succeed has been an important factor in my career.

What early experiences helped shape your interest in medicine?
My parents are both physicians who practiced medicine in an academic environment. My father is a physician-scientist and medical educator, so his career definitely served as a role model. I was always an educator at heart in my training years, though. It was not until I became a cardiology fellow at UCSF that I really began to pursue a research-oriented path. My co-fellows at UCSF were outstanding, and it was the interaction with them and...
several wonderful faculty members that led me to pursue a career in cardiovascular research.

What about cardiology especially appeals to you?

I really love cardiovascular physiology, and that as cardiologists we can see changes in physiology right before our eyes — on an echocardiogram, heart MRI test, or in the cardiac catheterization laboratory where we make invasive measurements of pressures within the heart. The fulfillment of the work I do comes from helping sick patients in need, educating trainees at all levels, and performing diverse types of research. I also enjoy attending specialized scientific symposia and advisory board meetings with other heart failure experts. I learn a tremendous amount from these sessions where our discussions can shape our field through clinical trials and other research studies.

Did you ever consider an alternative career?

I really wanted to be an actor when I was a Northwestern undergraduate, during which time I took theater classes. Several of my college friends were pursuing their Hollywood dreams, and I felt like it was the right time for an Indian-American actor to make it in Hollywood. But I wasn’t brave enough to give up my guaranteed admission into Feinberg — I was an HPME student — and I didn’t have much acting talent!

You’ve described heart failure disease as a “complex, heterogeneous clinical syndrome.” In lay terms, what does that mean?

Congestive heart failure is a syndrome, not a particular disease. It’s the end result of a variety of heart diseases, and a leading cause of death and hospitalization as we get older. We have typically treated heart failure using a one-size-fits-all approach; however, we now know that heart failure is heterogeneous and that we will likely be more successful with novel therapies if we match the mechanism of action of a new treatment to a particular type of heart failure patient who is most likely to benefit.

Your research is addressing this heterogeneous challenge by deploying data analysis to better understand heart problems.

You’ve used “phenomapping” to gain greater clarity about different kinds of heart disease. Can you connect the dots for us?

I think an analogy to cancer is helpful. These days, a tumor is removed, the tumor cells are analyzed, and the specific cellular and genetic abnormalities can be targeted with specific medications. We’d like to do the same in cardiology, but we don’t have access to heart biopsy tissue in most cases. Thus, we need to use indirect methods to figure out how to target medications to particular patients. Fortunately, we have laboratory and imaging tests that we use to obtain extensive data about how the heart and blood vessels are functioning in heart failure patients. Phenomapping is the use of machine learning methodologies to analyze the large amount of data to find patterns within the data that might identify groups of patients that are likely to respond to specific therapies.

You’ve said, “The future of clinical medicine will be humans and machines working together.”

What’s the potential of machines to advance medical science?

Machines can help us in many ways, and are already revolutionizing many industries: think of self-driving cars or voice recognition. Examples of promising ways that machine learning can help us in the future are 1. scouring electronic medical records to identify patients for clinical trials or helping diagnose rare diseases earlier; and 2. probing fundamental disease biology by integrating data from multiple sources — electronic medical records, imaging tests, and various “-omics,” such as genomics, transcriptomics, proteomics, metabolomics, etc. Then finding patterns within that data to help us understand disease mechanisms and target therapies to specific patients.

Machines may identify novel patterns within patient-level data that make clinicians say “A ha!” This can result in discoveries of novel disease patterns that may help lead to new disease classifications and therapy. Basically, machine learning may function like corrective lenses that allow clinicians to see more clearly so that they can prevent, diagnose, and treat diseases and clinical syndromes more effectively.

What do you see as the key challenges to integrating technology — including data analysis — into mainstream clinical practice?

Medicine today is a very fast-paced environment, and physicians tend to stick with what they know. Big data analytics must be understandable to the end-user — the physician and the healthcare team — and must be lightening fast to keep pace with the clinical environment. Once these things happen, and there is seamless integration within the medical record, for example, I think that clinicians will use these tools. In cardiology, we have embraced a large variety of cutting-edge technologies over the last 50 years. I fully expect that the same will occur with machine learning and big data analytics.

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