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Q1 **Most of your career has been devoted to understanding heart failure. What initially drew you to this complex area, and how has the field evolved since you began your work?**

I've been in the field for a long time. What first drew me to cardiology, and then to heart failure, was the ability to treat people and make them feel better. As a medical student, I remember diuresing dozens of pounds of fluid off a few patients in a week; I loved seeing them feel so much better at the end, and that was before we had today's modern, effective therapies.

I've now been involved in trials for 25 years, and watching new therapies improve both the quality and duration of life has been incredibly gratifying. I always say I have the best job in the world. We care for people in shock, people who are dying, people who are critically ill, and we have tools that can save their lives. But we also build long-term relationships with patients over years, even decades, helping them to feel better, stabilise their disease, and achieve their goals. It's the best of both worlds: the acute, exciting care of cardiology, and the long-term, meaningful connections with patients.

Q2 **Recent research has shown that heart failure with preserved ejection fraction (HFpEF) disproportionately affects women. How should this influence both trial design and therapeutic strategies?**

It's very interesting. I think that normal cardiovascular function in women is quite different from that of men, and we haven't studied or fully appreciated that. One of my favourite studies, by Susan Cheng, Cedars-Sinai Medical Center, Los Angeles, California, USA, and colleagues in California, USA, looked at blood pressure and cardiovascular risk.[1,2] For men, a blood pressure of 120/80 seems normal. For women, the 'normal' level is probably much lower. Women with a blood pressure between 100 and 110 already have increased cardiovascular risk, yet we still treat them when they reach 120/80, which may actually be a high blood pressure for many women.

Similarly, I think a normal ejection fraction in women may be different from that in men, but we don't know because it hasn't been studied. I'm very interested in learning what is truly normal for women across the lifespan. That may help explain why women disproportionately develop HFpEF. Part of it is longevity, as it's a disease of ageing, but I suspect there's more to it.

I know people criticise the under-enrolment of women in trials, but I think we've done reasonably well. Women are less likely to participate in research for complex reasons tied to their lives. Still, reduced ejection fraction trials usually enrol 30–40% women, which matches the prevalence. For

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preserved ejection fraction trials, if you take an ejection fraction ≥50, enrolment is typically 45–60% women. That may be a bit low, but it's still solid representation.

I would love to see more women in trials. Companies sometimes say, 'we provide childcare', but women in their 70s with heart failure don't need childcare, they need husband care. Many are caregivers not just for children, but for spouses and family. That burden makes trial participation difficult, especially with heart failure. We need innovative ways to lower those burdens while still learning what we need to know.

I'm hopeful about the future. We now have effective therapies for HFpEF that reduce hospitalisations. Over the course of my career, I'd like to say that I've developed many interesting hypotheses, most of which I've disproved. But that's science: slowly, steadily, we discover what does work.

It's also important to talk about awareness. When women are diagnosed with heart disease, they're often shocked to learn that it's the number one killer of women. That's because women don't talk about it. Women with breast cancer share their diagnosis; everyone knows. But women with heart failure keep it quiet. Part of that is due to the stigma that heart disease is the result of bad habits. However, age is the biggest risk factor, and none of us can avoid ageing. I hope that we can relieve some of the shame and encourage women to talk about heart disease, thereby raising awareness and increasing research participation.

Q3 As a leader in clinical trials in heart failure, how do you see socioeconomic status influencing both trial design and outcomes? Are we doing enough to ensure inclusivity and real-world applicability in large heart failure trials?

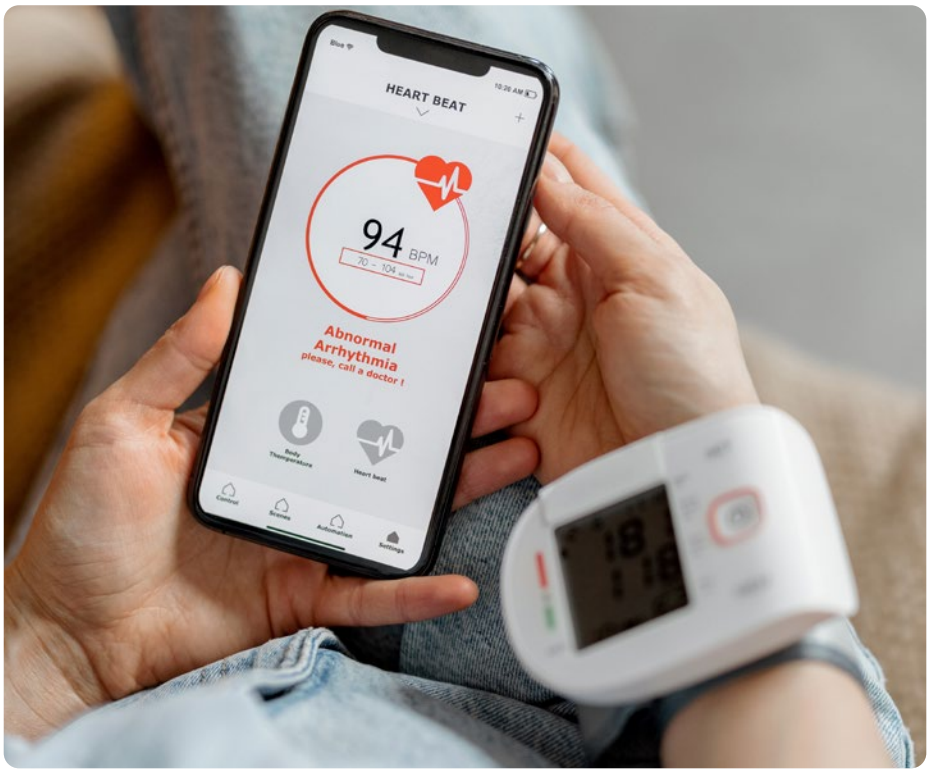
The short answer is no; we're not doing enough. Socioeconomic status affects everything. If you have food or housing insecurity, the last thing you can do is participate in voluntary research. Yet cardiovascular risk disproportionately affects people with socioeconomic disadvantages, and we need more resources devoted to that problem.

I practice in St. Louis, Missouri, USA, a city with a troubled history around race and inequity. We've done well enrolling minority and some disadvantaged patients in trials, but the truly disadvantaged, those facing multiple insecurities, can't participate. They simply don't have the capacity. Is it the pharmaceutical industry's job to solve that? No. Society has to solve it. Unfortunately, we're not solving it right now in the USA.

Q4 Left ventricular ejection fraction has long been the cornerstone for diagnosing and classifying heart failure, yet it captures only part of the disease spectrum. How can advances in imaging techniques overcome the current limitations?

Ejection fraction is a very crude measure, but understanding systolic function and cardiac performance in a more sophisticated way is helping us. At the European Society of Cardiology (ESC), we've seen exciting science around global longitudinal strain as a marker of subclinical systolic dysfunction. Many patients who have HFpEF, for example, have subclinical systolic dysfunction.

Some of my early studies showed that, while these patients look normal at rest, the heart can't mount the increase in cardiac output it needs under stress. Stress testing with sophisticated cardiac



assessments done in settings of exercise or pharmacological stress can unmask this, but these assessments are not routinely done. Imaging is getting better, and we're better at diagnosing subclinical systolic dysfunction, but I'm still waiting for a study that enrols people with abnormal strain and uses improvements as an endpoint, ideally coupled with heart failure events. Whether the FDA or other regulators will accept improvements in strain as an endpoint, I don't know, but we need more data.

In HFpEF especially, you can have a small ventricular cavity with a thick wall. That gives you a normal ejection fraction, yet very abnormal contractility. Strain may be the best way to show that there is systolic dysfunction, even though we call it a 'normal ejection fraction'.

Q5 A significant portion of your research has focused on cardiogenic shock, and last year you published a paper on the impact of mental health on cardiovascular outcomes. What can clinicians do to ensure more holistic patient care for these patients?

I've been trying to study cognitive function in heart failure, but our funding agencies aren't optimally set up for multidisciplinary work, so it's hard to find reviewers with the breadth to evaluate it.

One of the reasons I chose to focus on heart failure is because we care for the whole patient. We're cardiologists, but also internists, and we like it that way. When a patient isn't thriving, we look for all the reasons and use the resources available, because heart failure is expensive for health systems, and that gives us leverage. However, there aren't enough mental health services anywhere in the world. Depression and anxiety are very common in heart failure.

When caring for patients, I try to optimally treat all barriers to ideal health, try to get every affected system treated optimally, but that often means my patients have ≥6 doctors. In the USA, with our fragmented care, that's overwhelming. A general practitioner with 10-minute visits can't manage heart failure alongside six comorbidities. Our systems simply aren't set up to care for ageing patients with multiple chronic diseases. Over the next two decades, as populations age, this is going to explode, and I don't think any health system is prepared.

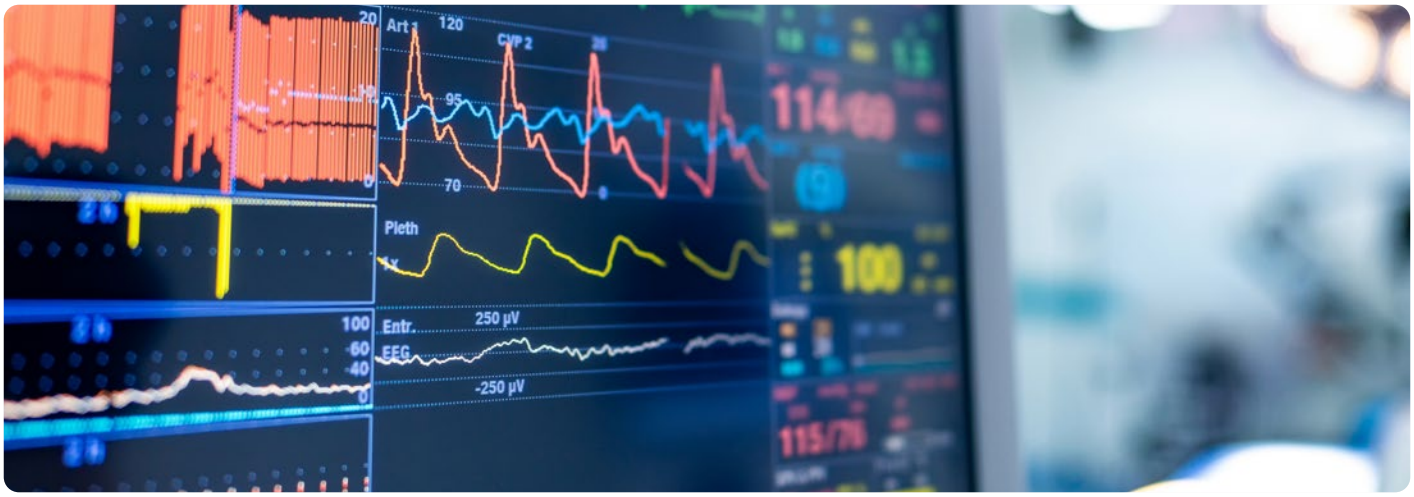
Is there any short-term solution for this, or does systemic change need to happen?

Systemic change is needed. Unfortunately, the first thing that will happen is that patients won't do well. I hope the 10-minute visit goes away. In the USA, there are some moves towards allowing 30-minute visits if you're managing a complex chronic disease, but the payments still don't match procedures like stents or ablations. The incentives are skewed. Hopefully, as the burden of disease grows, public health leaders will recognise that reactive care isn't sustainable.

Q6 At ESC 2025, you chaired the session, 'Heart–brain–kidney axis and beyond in heart failure'. Can you tell us more about this fascinating topic and the key take-home message?

It was a really interesting session. We kept coming back to the chicken-and-egg questions: is the heart making the kidney worse, or is the kidney making the heart worse? Is the heart driving brain decline? Is malnutrition making heart failure worse?

In today's omics world, we drill down to cells and molecules. However, I'm a physiologist at



heart, and physiology is about how systems interact: kidneys and heart, brain and arteries, heart and metabolism, etc. Is it abnormal haemodynamics leading to cognitive decline? Is it inflammation? We have to address these questions at a systems level.

It's an exciting time. Take the glucagon-like peptide-1 (GLP-1) agonists: they reduce inflammation, improve heart failure, and also cause weight loss. But is it the weight loss that matters, or the anti-inflammatory effect, or both? These drugs, developed for other purposes, have become natural experiments that are helping us learn. The session today featured young scientists with excellent data who are slowly chipping away at these complex problems.

Q7 Precision medicine and digital health are rapidly influencing cardiovascular care. What do you see as the most promising emerging tools for improving outcomes in heart failure?

There's still a lot of work to do. In HFpEF, we don't fully understand the disease. It's likely not purely cardiac, but systemic, maybe in part due to accelerated ageing. In some patients, it's driven by obesity or metabolic issues, and in others, by hypertension or subclinical systolic dysfunction.

Over the last decade, there have been a lot of efforts around phenotyping patients and tailoring treatment. But I'm not convinced that we've truly defined the mechanistic phenotypes yet. Trials are now being designed around specific phenotypes of HFpEF, but we haven't shown whether that leads to improved outcomes. Nonetheless, it will be fascinating to see where this research trajectory goes. As I've said before, much of my career has been built on great hypotheses, many of them disproved. We may find that some of the phenotypes that we're targeting aren't the right ones, but that's the scientific process.

Digital health is also very exciting. People are collecting more health data than ever, though right now it tends to be healthy people. It will be interesting when patients with chronic diseases start generating that data, which we can then interrogate and learn from. Even at this meeting, I uploaded an app that can estimate my risk of systolic dysfunction with an Apple Watch (Apple, Cupertino, California, USA) ECG. With AI, wearables, and apps, we'll have enormous opportunities for earlier and easier diagnosis. But again, it comes back to socioeconomic disparities. These tools tend to reach higher socioeconomic groups. The challenge is making sure that digital strategies reach the populations who need them most. That's a big societal issue we still need to solve.

Q8 You've dedicated a lot of time to mentoring and training young cardiologists. What advice would you give to those entering the field?

At this stage, my greatest satisfaction comes from helping young cardiologists and physicians build careers in clinical research. Those of us in clinical practice see unmet needs most clearly. We're well-positioned to ask the right questions, then develop the skills and tools to design studies, gather data, and move the field forward. One question leads to another: it's self-perpetuating.

As a journal editor, the papers I love are those with a clear hypothesis, good data, and a compelling story, whether the hypothesis is supported or unsupported by the data. That kind of science leads to more questions, more clues, and more studies: work that points the way forward.

For me, I've always kept both parts of my career alive: patient care and research. I love medicine and I love my patients, but I'm never happier than when I'm diving into new data and seeing what clues they hold. That's the excitement I try to pass on to young people: stay curious, ask great questions, and keep both the science and the patient at the centre of it all.

References

1. Ji H et al. Sex differences in blood pressure associations with cardiovascular outcomes. Circulation. 2021;143(7):761-3.
2. Ji H et al. Sex differences in blood pressure trajectories over the life course. JAMA Cardiol. 2020;5(3):19-26.