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The Biomechanical Approach to Heart Disease

### BIOMECHANICAL APPROACH TO VARIOUS TYPES OF HEART DISEASE

You are listening to ReachMD XM160, The Channel for Medical Professionals. Welcome to medical breakthroughs from the University of Pennsylvania Health System with your host Northwestern University internist, Dr. Lee Freedman.

**The biomechanical approach to heart disease. What is it and how might it change our approach to common cardiovascular diseases? With me today is Dr. Joel Gorman, associate professor of surgery at the University of Pennsylvania School of Medicine and co-director of the Gorman Cardiovascular Research Group.**

**DR. LEE FREEDMAN:**

Thank you so much for being with us, Dr. Gorman.

**DR. JOEL GORMAN:**

Thanks for inviting me.

**DR. LEE FREEDMAN:**

Can you start by telling us what is the biomechanical approach and how does it differ from the more traditional approach used by most investigative groups?

**DR. JOEL GORMAN:**

Our group is interested in, you know, structural heart disease, basically heart failure and valvular heart disease and a lot of groups have approached the treatment of particularly a heart failure in a way that's pretty reductive, they try look it at a genetic level or biochemical level, but when you break that particular disease process down that far, you have trouble translating your findings back to a clinical treatment that actually impacts the patient. You can say for a gene that affects heart failure or biochemical process that you know is associated with a pathogenesis of heart failure. It has been shown that it is hard to really take those findings in impact on really the

treatment of patients with heart failure.

DR. LEE FREEDMAN:

No real practical therapeutic application at least yet?

DR. JOEL GORMAN:

Right. So basically what we try to do is to kind of assess the problem at an organ level. You know you are looking at the whole heart and you know how can we intervene or how can we set up experiments that allow us to understand the pathogenesis of the disease process at that level and then intervene at that level because our group is where physicians or surgeons, but where most of us are engineers, so we have kind of a mechanical bent to our background and you know we feel that understanding things at the whole organ level is valuable and that it allows us to deal with things we understand more completely than the biochemical and the genetic makeup of our mechanisms of disease. It is kind of like some investigators that work and we would like them to taking a planer part to try to figure out how it works and you find out a lot of stuff, but then sometimes its going too hard to put it back together and get a plane that works again.

DR. LEE FREEDMAN:

Very interesting and it does sound like for this type of approach either engineering or physics is an important part of the background. Is that the case?

DR. JOEL GORMAN:

That is the case and like I said almost all of our members have not only a medical background, but an engineering background.

DR. LEE FREEDMAN:

And are there particular heart diseases that you are looking at with this approach?

DR. JOEL GORMAN:

Our group has basically 3 big overarching areas of interest and many sub interests under those big headings and the 3 major interests are the pathogenesis and treatment of heart failure, valvular heart disease, and then cardiovascular imaging.

DR. LEE FREEDMAN:

And to have an approach like this are standard diagnostic tools adequate or do we need to look at certain other imaging techniques or other techniques to understand this biomechanical approach?

**DR. JOEL GORMAN:**

Yeah. I think all of our research is problem based and when we start out with an important clinical problem or important clinical disease that we feel doesn't have a satisfactory treatment in our eyes and then try to apply our engineering and medical and surgical skills to developing novel processes for treating those diseases and heart failure is probably prime on the list and that the type of heart failure that we are really interested in is type of heart failure that affects millions of people throughout the world and that's postinfarction heart failure. Patients who have the heart attack and don't have heart failure initially, but the infarction causes a remodeling stimulus on the rest of the ventricle and over time months or years causes them to go into heart failure and ultimately die and right now we are as physicians and certainly surgeons, but we are very bad at treating patients once they have developed heart failure. There is a whole bunch of medications, they kind of palliate it, and then we as surgeons that you know being kind of impatient by personality have decided that you know maybe there's something we can do surgically and over the past 5 or 6 years, many aggressive operations to treat heart failure by reestablishing normal left ventricular geometry have been proposed and really have met with very limited success. So our group has become very pessimistic that you can really ever treat postinfarction heart failure once it is established and we really think that you have to jump on the disease early and prevent it after an infarction and that's a nice concept, but its for with a lot of difficulties and a lot of difficulties can be our cardiovascular imaging problems because you have to identify patient, not everybody has a heart attack ultimately goes into heart failure. So you have to have realistic or reliable imaging techniques and ways to assess those imaging techniques that tell you who is going to on to remodel and going to have heart failure after a heart attack, so you can intervene early.

**DR. LEE FREEDMAN:**

Sounds like ultrasound would be a very good way to try to assess that we have the tools to assess who might be at risk for going into heart failure.

**DR. JOEL GORMAN:**

Yeah, I think we are on the cutting edge of that right now and in our laboratory we do a lot of work with real time 3-dimensional echocardiography and MRI in an attempt to try to identify or come up with criteria using those imaging techniques to identify people that will ultimately go into heart failure.

**DR. LEE FREEDMAN:**

And imagine those type of studies or looking at that is going to take sometime to see if people do go into heart failure and what characteristics that you have come up with?

**DR. JOEL GORMAN:**

That is very true, but where we also have a very strong advantage in our group is that we have developed several very realistic large animal models of post infarction ventricular modelling may lead to heart failure, so we can manipulate that model to mimic the human disease very precisely and then we can bring to pair some of our imaging technology on to those models, which while not perfect, gives us an even stronger educate to guess as to what will work in the human, so you know for what is just purely a fishing expedition where you were just imaging people and trying to correlate with their ultimate outcome, you may find it difficult, but with the animal models we can kind of educate ourselves as to what we should be looking at in the humans.

DR. LEE FREEDMAN:

And are there specific parameters that you have identified at this point?

DR. JOEL GORMAN:

It gets a little complex, but we have an infarction as we all know that that part of the ventricle stops working, but what happens is that there is an area of myocardium around the infarct that's normally perfused that we call the border zone, that even though its normally perfused, it undergoes geometrical distortions and dysfunctions due to the kind of black hole of the infarct. The infarct kind of pulls on it as it stretches, and we found that there are certain criteria or geometrical changes within that borders on that you can assess with 3-dimensional echocardiography, and MRI that give you some predictive value as to who is going to ultimately go into failure or not. There is really kind of a paradigm of how imaging plays against the therapeutic intervention that you want to carry out. Now, you know, what we are doing is as surgeons, you know, can become very aggressive and we can make all kinds of incisions, that we can expose the heart and do really whatever we want to it, but when you don't know who is going to go into failure if that kind of limits how aggressive you can really be, so if you have an imaging technique that's very precise and tells you that I know 100% that this patient is going to into failure some 6 or 7 or 8 months down the road, then you could potentially be justified in saying well, you know, we can apply an aggressive surgical procedure to this person because we know he is going to into heart failure, but we really don't have that at this point, but you can work at it from both ends. If you look at it from the other end, now if you have a minimally invasive procedure or catheter-based procedure, we don't really inflict that much morbidity, then your ability to predict, who is going to go into failure becomes less. So if I say I have a catheter-based therapy that's not really going to hurt anybody, that's potentially not going into failure, but its going to help a lot of people that are going into failure, then I can get away with a less precise imaging modality, something that gives me an educated guess, may be good enough to apply a less invasive therapy whereas if you have a more invasive therapy, you need a much more precise predictor on your imaging technique.

DR. LEE FREEDMAN:

If you are just tuning in, you are listening to medical breakthroughs from the University of Pennsylvania Health Systems on ReachMD, The Channel for Medical Professionals. I am your host, Dr. Lee Freedman and with me today is Dr. Joel Gorman, associate professor of surgery at the University of Pennsylvania and we are talking about the biomechanical approach to various types of heart disease.

So Dr. Gorman, with 3D real time echocardiography and MRI, we are developing some parameters that might have some predictive value. Can you tell us more about these therapeutic approaches for post MI and perhaps for other heart conditions?

DR. JOEL GORMAN:

Sure, there is a kind of a descriptive term that we would like to apply to a lot of what we do and we would like to think of ourselves as developing catheter-based techniques for the treatment of structural heart disease and structural heart disease meaning really heart failure and valvular heart disease and we are in the process of developing methodologies that would allow us to deliver certain substances to the heart after a myocardial infarction that would allow us to influence the material properties of the infarct to prevent that stretching and to prevent those ongoing distortions, and we are looking at a variety of substances from stem cells to other nonliving substances or structural-type substances that allow us to stiffen the heart and prevent remodeling. We are also looking at catheter-based techniques for repairing or replacing heart valves particularly you know the mitral valve.

DR. LEE FREEDMAN:

And so for the post MI, through a catheter you would deliver stem cells or some other substance to prevent that remodeling that would eventually cause heart failure and mitral valve repair is that something that is still in the experimental stage or we are seeing some of this applied in clinical practice?

DR. JOEL GORMAN:

We are starting to see the first ways of the development process coming to clinical application that we have been involved in some of the mitral valve repair techniques that are starting to you know come to clinical trials. That was the work we kind of did in the early 2000s and we are starting to see some of those clinical trials now or what we are actively involved with now is not so much repairing the mitral valve, but actually looking at the feasibility of replacing the mitral valve through a catheter-based technology, and we have kind of developed a development paradigm for that process to is where we take a technique. We think we can ultimately get through you know place through a catheter, but early in the development process we don't set the bar that high. We try to bring the technology along where we develop it to be placed via a small incision without cardiopulmonary bypass and then once we have achieved that, we start working on catheter-based strategies to place that same device and we are working currently on 2 or 3 technologies to replace the mitral valve using that development paradigm.

DR. LEE FREEDMAN:

Eventually could this be applied to other valves you feel or?

DR. JOEL GORMAN:

Right now, on the market there are 2 technologies that are in clinical trials for the replacement of the aortic valve. The aortic valve is probably a little bit easier. The mitral valve presents even more challenges due to its more complex anatomy and its relationship with the left ventricle. The aortic valve is a simpler anatomy; as you know it's a 3-cusp valve within a cylinder, so you know, it's amenable to stented valve replacement technology. With the mitral valve, we are finding that the design has to be a little bit more complicated.

DR. LEE FREEDMAN:

I would like to thank my guest from the University of Pennsylvania School of Medicine, Dr. Joseph Gorman, who has been outlining for us some exciting new techniques from a biomechanical approach that may be used in congestive heart failure particularly post MI and with valvular heart disease and even with coronary artery disease, the most common type of heart disease that plagues us here in the United States.

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