AEHA
ASSOCIATION FOR ERADICATION OF HEART ATTACK

Transcript of the discussions at the 2nd Vulnerable Patient Symposium
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New Orleans, LA

DISCUSSION PANNEL

Moderator: Morteza Naghavi, MD

Panel Members (left to right): Leslee Shaw, Ph.D., Alan Taylor, M.D. Pedro Moreno, M.D., Jagat Narula, M.D., Dan Berman, M.D.,

DR NAGHAVI

We're going to have a few minutes of remark by Dr. Moreno, who has been a member of the first Vulnerable Patient Symposium and we had discussions on the concept of risk factors versus risk markers, if Pedro remembers. We were talking about what do we do for the detection of hypertension? We know how many risk factors contribute to hypertension. Are we measuring endothelin or are we measuring plasma renin activity? Are we measuring angiotensin in these patients? No, we're not. We're just measuring a simple cuff-based based marker of a systemic disease. Blood pressure is not a disease of the right arm.. We have found a bio marker, an easy and inexpensive one and I'm sure if you put that in the model, Dr. Taylor will tell you that model will be successfully cost effective. We are looking for something like that for the bottom of our

pyramid in order to cost effectively start a screening. And that is the beginning. Pedro, I'd like for you to give us a few minutes of your comment.

DR MORENO
I'll be very brief.

DR. NAGHAVI
Go ahead.

DR MORENO
I'm very impressed with the comments done tonight, and honestly, I'm not a cost effecting this person. I'm a clinician and I do interventions. I'm focused on secondary prevention, which I'm more concerned about actually because the primary prevention, even though we have patients that occasionally are refered to us to do primary prevention, it's in the field of health care and a very bottom line, and probably not even physicians -- general practitioners maybe. So, I see this problem more on the education in sending a message for a traditional approach to good medicine initially. On the secondary prevention, it's a different story and we already heard about it specifically with Cath lab techniques and all those. So, to be honest with you, I still see the field a little bit confusing regarding the magic "Holy Grail," you know, test that will identify the patients that will end up with having an event.

DR NARULA
And I don't think that I can really talk of the cost effectiveness here because what I do is I fantasize and I just dream and I sell dreams. We've been working on various nuclear strategies, which try to identify the vulnerable plaque. And I believe that obviously the inflammatory markers that do go a long way with the bottom markers go a long way, but eventually the identification of vulnerable plaque is something which cannot be ruled out. And one really needs to look at the vulnerable plaque. And our belief is that one can really look at the macrophages in the plaque. If we have these properly designed targeting strategies. We can look at the macrophages which are undergoing cell death, and once they're undergoing cell death, they are likely to make the plaque vulnerable because if it's likely that they release the metaloproteinases. So, we can identify macro phages. We can identify the cell death or the apoptosis. One can also noninvasively try and identify the release of metalloproteinases, which eventually could lead to the vulnerability of a plaque. Thank you.

DR. NAGHAVI

Thank you. We're going to have Dr. Berman for his few minutes of comments and then I'm going to go back to Dr. Shaw for a conclusion.

DR. BERMAN

Well, thanks for the opportunity to say a few words. It's been a very interesting symposium. I completely endorse the concept of eradicating heart attacks. I think the Association for the Eradication of Heart Attacks is an excellent association for us all to become involved in. I, looking at the evening, I agree with most of the speakers and am fortunate to be in a position of running a cardiac imaging section where we do EBCT and we do nuclear testing and we do PET and we do CT angio and we do MRI. And in looking at that spectrum, my view of the pyramid coincides with much of what was said. I would point out that I think at the present time, when we look at cost, that maybe we have to be careful about how far we stretch that lower limit of the intermediate risk group that might need testing.

We noticed earlier Dr. Braunwald and Dr. Fuster both used a 0.5 percent per year limit, which is even lower than the .6 percent that Dr. Taylor's group came up with, but it was reluctantly they came up with it because at 10 to 20 percent is something that would be more reasonable when we look at the proportion of the patients who would be tested and the risk of those patients. We're probably going to have to , in view of limited funds and be aware of that kind of limitation. But I think starting within the intermediate risk group, an acceptance of the value of testing is a good starting place that our society hasn't yet reached. If you're in the Army, you might be able to get this test, but if you're not in the Army, you have to have $400 of spare change to be able to purchase the test because our third-party carriers even in this clearly defined 10 to 20 percent risk group won't pay for the test.

Then we go on to the need for further testing. And I agree with the earlier comments that MRI has a big future. I think CT in geography has a future. I think nuclear testing has a future. Exactly where they're going to fit in has to be defined. I found that the discussions about cost effectiveness very, very interesting. And just to kind of pull it all together, I think we're all in the same team. And Dr. Callister (phonetic) actually should be joining us up here on the panel because he's one of the leaders of this team whose data has shown us how dramatically the knowledge about coronary calcium can predict subsequent outcomes. But in pulling it all together, I do think it does come back to this: What is going to be the effectiveness of finding the early disease? And if this new organization is right, then maybe the assumption that we will be causing a 30 percent reduction in mortality will actually be wrong. And in the future, perhaps we will be reducing that mortality by not 30, not 35, maybe 40 percent, maybe 50 percent, maybe

even farther, at which time then, we'll have a marked difference in these cost effective analyses as was so nicely pointed out by Dr. Taylor.

DR. NAGHAVI

Thank you very much. The last few seconds of the meeting, I'd like to go back to Dr. Shaw and ask her if you had a wish for a screening test to start from the bottom of the Pyramid, what would that test be and how much that would cost?

DR. SHAW

Well, the goal would be that you would want a test which was -- it would be as effective as it could be, but it would be optimally as inexpensive as it could be. Paralleling other test costs, it would be at a minimum -- now, it depends on your perspective, but from a societal perspective, it would be a hundred dollars or less.

DR. NAGHAVI

Less -- less than a hundred dollars.

DR. SHAW

In some of the cases when you think about MR, applied to that 40 million people, that would be cost prohibitive in large part because of the amount of induced medications and procedures that could follow that. But certainly I think calcium screening is in that range. We need a lot more data. Some of the laboratory markers are in that range and that would be a very effective place to start.

CONCLUSION

DR. NAGHAVI

Great. Thank you. Well... I, initially at the beginning of this meeting, I mentioned this to you and I'll give you a quick report of how many patents are out there on “Polypill”. There were -- the last time when I counted it was about a hundred and thirty patents on “Polypills”. They're aggregated to each other. And the way I see it, there are actually every day -- every week, Tuesday, if you get on US patent database, you'll see about 30 to 40 new patents related to atherosclerosis. And I'm amazed to see more than 50 percent of them are related to “Polypills”. This is what I anticipate will be happening. As you know we are scientists in the academia, but the ones who are actually leading and pushing everything is industry and the money is driving us towards “Polypill”. There is a reason for that. 'Cause these drugs, if you accumulate them, the magnitude of the effect Dr. Berman, will be more than 30 percent. We're going to see that. Why? Currently you have only statin and at the very top of the Pyramid, you have drug eluting stents. Dr. Serruys showed you how he exercised drug eluting stents and his patients

were doing very well. Now, you've seen Steve Nissen's data with injection. You've seen new data from Allen Fogelman and Navab and recently from P. K. Shah's group that we are having oral HDL therapy basically, which will give a far greater effect than statin therapy.

So, that's where we can really see the vision of putting America in SHAPE is based on what we are building. Now, we have two parallel efforts with AHA's leadership and collaboration with others. One is at the CT level. I look forward to getting the chance to updating you while you're presenting the effectiveness or ability to detect and that is to image vulnerable patient, not just one vulnerable plaque. And there is a long list. You will see a few presentations during this conference that you can add to the predictive value or diagnostic value of the CT. You have much more information than an average calcium score you're reporting. And we're not using this information. And if you put them in proper model, we will be able to enhance the predictive value of the test, which you're actually doing right now, which you're paying for those studies. You take the radiation already.

The next level, which Dr. Moreno will be talking about tomorrow, it's what we call "Ultimate IVUS" It's a project again with the same nature. With IVUS, you collect so much data. A lot of those data are not being used. Dr. Serruys showed you some of the wavelet analyses, but we, for example, injected microbubbles in the IVUS and we've seen an enormous enhancement with injection of microbubbles for vasa vasorum imaging. Now, what is vasa vasorum imaging? Here's the man who's going to present it the next few days and Dr. Fuster really inspired everybody in this field that maybe vasa vasorum imaging is better than macrophae imaging. The bottom line is we have IVUS already in our hands. How can we empower it? More -- get more from IVUS? We're paying for it anyway. We have CT in our hands. What can we do to increase the power of CT? The bottom of the pyramid is the mystery that I've been starting working with P.K. Shah and hopefully soon with your group and others that how can we find the biomarker that would be a risk marker, not a risk factor? Because we know that there are so many risk factors that we're not aware of. Now, with Proteomic we might find 50 more. We will find chips that are going to be sold out everywhere and they do all sort of proteomic assays, but is that really the way to go? Again, back to the analogy of hypertension, I think it's not. We're going to look for the cough test. We're going to have to look for that test that would be less than a hundred dollars.

With that, I would like to thank everybody participating in this meeting and I look forward to having the next meeting at AHA, American Heart Association. In the meantime, the SHAPE committee will have a small group meeting. We will invite our faculty for a trip

to Houston. Hopefully, at the time, it is not too hot. And we will be reporting that as a supplement to the *Circulation Journal*. Thank you very much. (Applause.)