SEX DIFFERENCES AND HEART DISEASE

Transradial Access in Women

Women at Greater Risk for Bleeding Complications in PCI

Cath Lab Digest ***talks with Jennifer Tremmel, MD, SM, Stanford University Medical Center; Director, Transradial Interventions; Clinical Director, Women's Heart Health at Stanford, Stanford, California***

How do women and men compare in risk for heart disease?

Heart disease is more prevalent in men than women, but remains the leading cause of death for both sexes. Cardiovascular disease, on the other hand, which also includes heart failure, hypertension and stroke, is more prevalent in women. Likewise, each year, more women than men die of cardiovascular disease. One out of every four women will die of heart disease, and one out of every two will die of cardiovascular disease.

Do you think most healthcare providers are adequately educated about women and heart disease?

There is definitely an increasing awareness, but I still hear physicians, particularly cardiologists, who come right out and say they don't think there is any difference between women and men in terms of heart disease. There is now over a decade of research that shows otherwise, and for a group that prides itself on evidence-based care, it is disheartening to hear such an inaccuracy being spoken. Certainly, patients notice. I've had plenty of patients come in and tell me, "Well, my doctor said there is no difference between women and men, but that doesn't sound right to me."

So patients also have a certain level of awareness. But is it enough?

It, too, is growing, and oftentimes patients are out in front of their doctors in this regard. Patients hear about the differences and it rings true, particularly for women. It's almost like they've been waiting for us to figure this out. They already have a sense that they are a little different, and sometimes have felt disregarded in suggesting something was wrong with their heart. We still need to educate ourselves and our patients so that awareness continues to grow.

What do you think of the Red Dress Project from the National Heart, Lung, and Blood Institute, and the Go Red for Women Campaign from the American Heart Association? Those seemed to have raised awareness.

Yes, I would agree. They are fantastic programs that have definitely raised awareness. The percentage of women who can identify heart disease as their leading cause of death has increased from 30% to over 55%. I remember the first time I saw an announcement, which was a fold-out ad with women in red dresses. It certainly caught my eye. It has been a very effective campaign, similar to the pink ribbon campaign for breast cancer. We need things like that to happen.

What are the considerations that must be taken into account when women undergo a coronary intervention?

In general, the gap in outcomes between women and men has narrowed over time, so that there is not much difference in terms of outcomes, with one big exception. Currently, the single most significant difference between women and men having a percutaneous coronary intervention (PCI) is bleeding and vascular complications. Women have two to three times the risk compared to men.

Why is that?

No one knows exactly why. There are several thoughts, and it's likely multi-factorial. One thought is that women have smaller vessels and may have multiple sticks, or more posterior wall sticks, which then increases the risk of bleeding. Another thought is that women's hormonal milieu results in greater vessel fragility. For example, we know women are more likely to get dissections due to estrogen levels, so maybe there is something inherent in the vessels themselves. A third thought is related to anticoagulant/antiplatelet dosing, and there is certainly some evidence of that, but at the same time, even if dosing is done correctly, women will still have a higher risk of bleeding and vascular complications.

The transradial approach is well suited for women, then, since it lessens bleeding and offers decreased vascular complications. Is that why you began to use it?

Yes, I specifically switched to transradial access for that reason. I take care of both women and men (about 70% women and 30% men), but as

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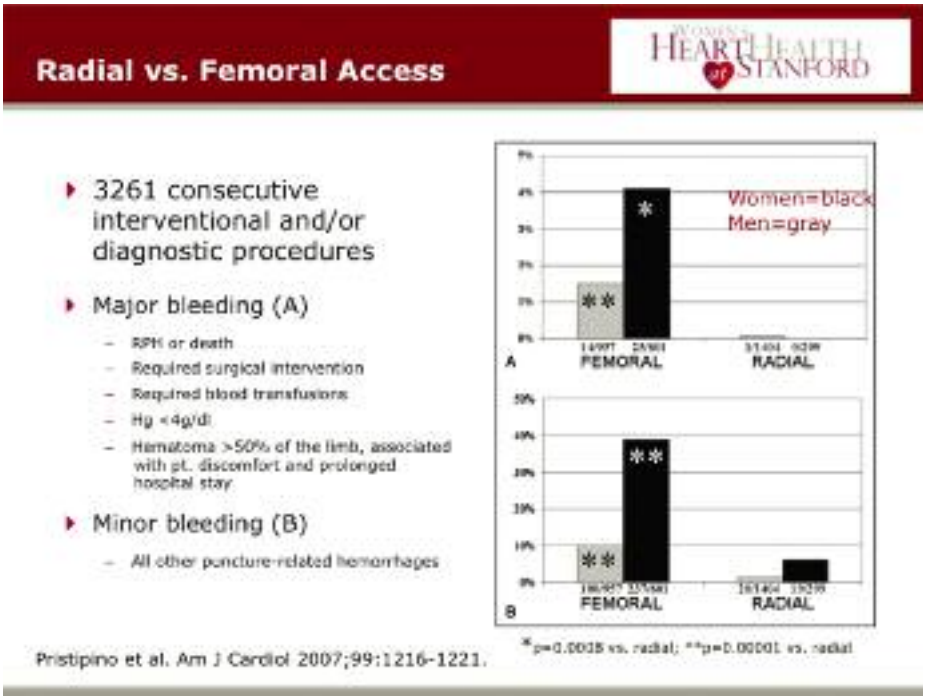

Director of our Women's Heart Health Program, one of my jobs is to improve the outcomes of female patients. Bleeding and vascular complications is certainly an area that needs improving. Since we don't know why women have more complications, it becomes difficult to address directly. Vascular closure devices certainly weren't the answer, and cutting back on anticoagulants and antiplatelet therapies wasn't the answer. It wasn't until I read an article discussing the reduction in bleeding complications with the transradial approach that I felt like I had found an answer.

What is the difference in bleeding between femoral and transradial access?

Transradial access offers significantly less bleeding, with a greater than 50% reduction in the odds of a bleeding complication. Since women have higher risks of bleeding at baseline, they drop down significantly in risk, nearly to the level of men, who also have a drop. But women are getting a much bigger bang for their buck, so to speak, in terms of their reduction in bleeding complications.

Can you tell us about your practice and research?

I am an interventional cardiologist. I am also trained in preventive cardiology, and I focused my broad training on women's heart disease. In doing so, I became interested in sex differences and how this information can be used to improve outcomes, for both sexes, but the group most in need of improvement at this point is women. For the last 50 years, our research data has been derived predominantly from men, and we have been applying it to women, thinking that it will give them the same benefit. What we have found out is that this is not the case. We need to use sex-specific data in treating our patients. My process is about taking the information that we have learned over the last decade or so about how women are different, and applying it to patients in hopes of improving their outcomes.

My research will hopefully contribute to that literature. I do research in sex differences in cardiovascular disease. My main research project right now is looking at sex differences in coronary pathophysiology. I'm looking at differences in women and men who present to the cath lab with symptoms consistent with angina but have normal appearing coronary arteries. We are testing to see if women or men have higher rates of endothelial dysfunction or microvascular disease, and also evaluating the distribution of plaque within their coronary arteries. While I'm doing this for research purposes, patients don't have to be in a research study to have vascular function testing, since these tests are clinically indicated in patients with angina, but normal appearing coronary arteries. During the angiogram is an opportune time to do this testing. It's not very satisfying to a patient to hear that everything is fine with your heart, and then get off the table and still have angina. Testing allows the physician to customize therapy based on the results. If we find everything is normal, then we are comfortable telling the patient that within the realm of what we currently know about coronary arteries, you don't have any problems. On the other hand, if we find an abnormality, we have a diagnosis that we can aim to treat. To me, it's worth the extra twenty or so minutes of testing. There are just too many people who continue to have their symptoms and no one knows what is wrong. These patients already had an angiogram, and sometimes two or three angiograms.

When we test for endothelial dysfunction, we administer acetylcholine directly into the coronary arteries. Acetylcholine, with normal endothelial cells, will cause the artery to dilate. If the endothelial cells have become dysfunctional, then the artery will paradoxically constrict. Endothelial dysfunction is different from coronary vasospasm. These are two different entities which are treated very differently. It's important to make the distinction, but people rarely do. Coronary vasospasm, or Prinzmetal's angina, is a smooth muscle cell problem, rather than an endothelial cell problem. It's much rarer than endothelial dysfunction, and while calcium channel blockers are very helpful for Prinzmetal's, they don't seem to provide relief to those with endothelial dysfunction.

To test for microvascular disease, we put a coronary pressure wire in the artery, give adenosine, and calculate the CFR (coronary flow reserve) and IMR (index of microcirculatory resistance). We are interested in the resistance of the

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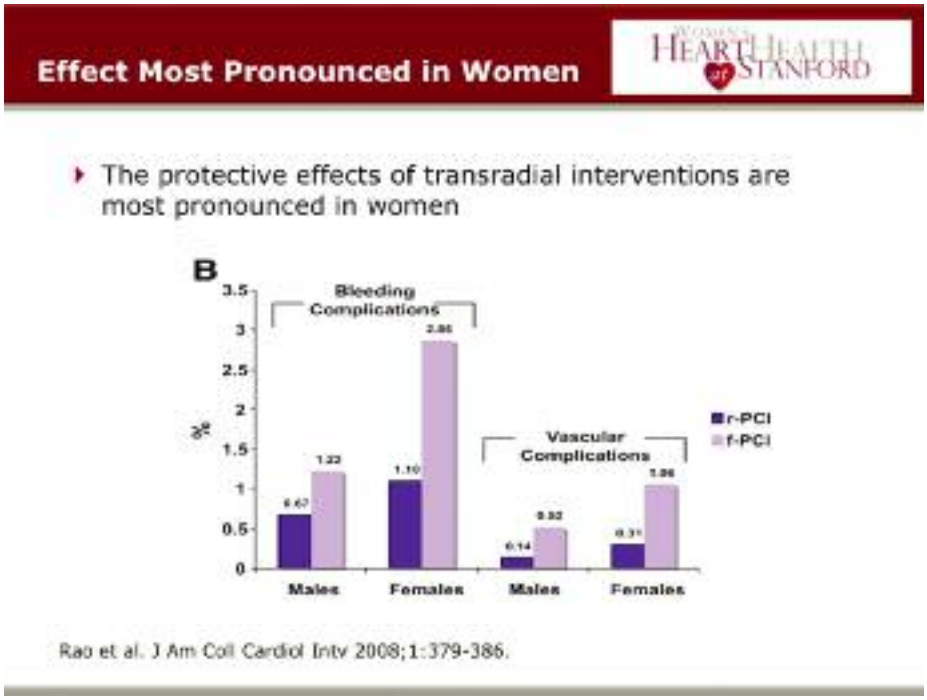
microcirculatory bed. If you have a healthy microcirculation, you have a low resistance, letting the flow go through very easily. On the other hand, if you have microvascular disease, the resistance is high. Finally, the distribution of plaque can be looked at with intravascular ultrasound (IVUS). Angiography can be deceptive. If there is diffuse plaque within the artery, a tight narrowing seen by IVUS may not have appeared so by angiography.

You mentioned that an article was the catalyst for you to get started with transradial access.

I read the article in early 2008. It was published late in 2007. Right when I read it, I had one of those "aha!" moments. I felt that this was the answer to my question on how to reduce bleeding complications. As it turned out, I was coincidentally offered the opportunity to attend a transradial course. I didn't even know they had courses. It was serendipity. I always say, when the student is ready, the teacher will appear. A Terumo representative happened to be in the lab and asked me if I wanted to go to a day and a half course in New York. Most of the courses are out east, which is something we need to correct here on the west coast. I took the course and felt comfortable very quickly that transradial access was something I could do. The course took away a lot of the mystery of the whole procedure. I came back and essentially just started doing it. I set up a cath lab nurse, technologist and holding room nurse as my core team and they went through this initial change with me. When I came back, I worked with my core team. Knowledge of what we were doing quickly started to disseminate through the lab, and we found the other nurses and techs were interested. In the beginning, I do think it was helpful to have a core group so everyone didn't need to be immediately educated. But it wasn't long before I gave an in-service to all staff in the cath lab and started training my interventional fellows as well. The fellows were very excited and started



scrubbing in on every case with me. They became very proficient. It took a few months, definitely. When we first started, it didn't always work, and we would sometimes have to convert to the groin, but we were persistent and we improved.

How frequently do you use transradial access?

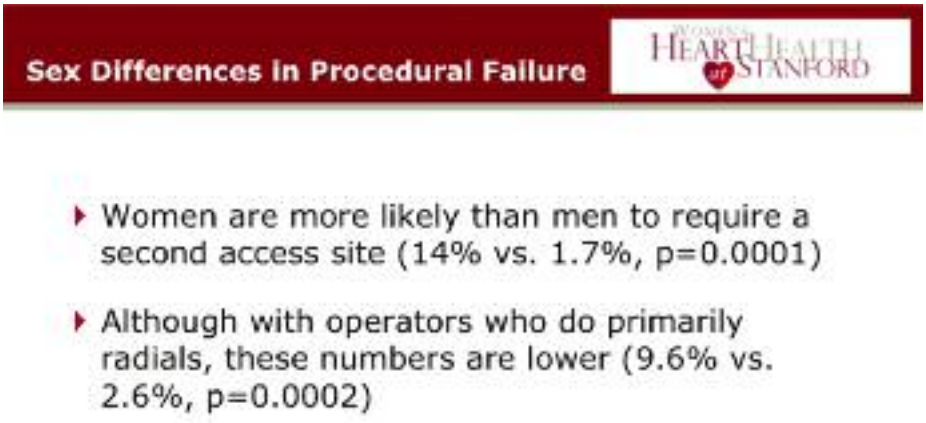
I use it 100% of the time, with rare exceptions. On occasion, I still have to convert to the groin. Conversion will happen to everyone at some point — there will be a reason you can't get access through the wrist. For my exceptions, if I know ahead of time that I want to use a large sheath, such as an 8F, I would start with the groin. If I know I need a balloon pump, I would probably start out with the groin, although I can still do the PCI through the wrist and then put a balloon pump through the groin, just as we might do the procedure through one groin with a balloon pump in the other. Otherwise, I don't have too many reasons to use the groin. We've done chronic total occlusions, bifurcation lesions, grafts, fully anticoagulated patients, rotoblator, you name it.

We recently began doing ST- elevation myocardial infarctions (STEMIs) through the wrist as well. We've done several and they have gone well. Transradial access hasn't delayed us at all. We're fast. But, we made sure we'd gotten good at the technique before we started with these patients, and if we ever run into a situation where radial access seems to be slowing us down, we'll simply convert to the groin. Since bleeding complications are highest in women, the elderly, and high-risk STEMIs, these patient groups are also the ones in which we should be making an effort to use transradial access.

One small obstacle is the significantly higher rate of needing to convert to the groin in women as compared to men. In those patients where you hope to use transradial access the most (women), there will be more conversion to the groin. Operators have to deal with that fact. It's not a very high conversion rate, roughly 10%. For the majority of women, you can successfully go through the wrist and lower their complication rate overall. With this in mind, we always have the groin and the wrist prepped, and if there are any problems, then we just go to the groin.

What have you observed in your transradial approach experience so far?

It's gone very well. I am lucky to be at a very wonderful institution that is very supportive. I was probably most



Pristipino et al. Am J Cardiol 2007; 99:1216-1221.

surprised by how much the patients like it. Understandably, patients are often frightened about their procedure, but for many, it's actually after the procedure that the worst part begins. They lie flat on their backs for several hours with someone mashing on their groin. If a groin complication occurs, the groin is held even longer, the patient has to lie flat even longer, and there's often a lot of pain. Eliminating femoral access makes a huge difference. Patients can get up right away. They can go to the bathroom, sit up, and eat lunch. We just don't see as many problems.

Have other physicians you are working with begun to use this approach and are you promoting it?

My colleagues have certainly become interested in transradial access and a few of them are starting to use it. I would be thrilled if everyone was able to do it. Partly because I've had an increasing number of patient referrals specifically for radial procedures, which is wonderful, but I can't be in the cath lab every day of the week. I welcome help from others in my practice who can provide that service. Patient referrals have gone up specifically because we can offer transradial access. The fellows, as I mentioned, have enjoyed learning it. They are fully trained and will go out in the world with this skill. When they are interviewed for jobs, they can point to it as a skill that they can offer, which I think is a plus for them.

What do we have to overcome to increase utilization?

First, physicians need a reason to do it. For the most part, the femoral approach has served interventionalists very well and we have come to accept a small risk of bleeding with our procedures. But we need to recognize that there is a way procedures can be done with an even lower risk of bleeding.

Second, physicians need to hear people requesting this approach. If patients hear about transradial access and ask for it, then that physician is going to pay more attention. In particular, if a patient says, I want to go to Dr. So-and-So because they can go in through the wrist and my bleeding complications will be lower, that may increase a physician's drive to learn and adopt the technique.

It's important to dispel the mystery here. The transradial approach is not rocket science. Our profession is set up as an apprenticeship, and fellows learn what the physicians before them have done. If these physicians aren't doing transradial access, then fellows are not going to learn it either. It's difficult for a fully trained interventionalist to step back and say, I'm going to learn something new and be in a position where I don't know everything again. There has to be a willingness and a reason in their minds that they are going to go back and train in something new. For me, it was the question of how to help lower bleeding complications in women. That question was what drove me. For someone settled in their practice, who feels happy with how things are going, it's going to be a harder sell until patients come in and ask for a change. I would also say that from what I've heard, the physicians who have been around longer and may have actually tried transradial access in the past often had a bad experience. So they are not necessarily willing to go through that again. But, importantly, the technology has improved, and getting access in the radial artery is smoother and easier than it used to be. Further improvement in the devices is yet another way to increase utilization.

What do you see as the future both for women with heart disease and for the transradial approach?

The future of transradial interventions is bright. It is something that is going to grow and take hold in the United States, just as it has in many countries around the world. No doubt, we're just seeing the tip of the iceberg.

Regarding heart disease, I hope that the gap between women and men will close, and just as men have enjoyed a decrease in their mortality from cardiovascular disease over time, women will see a reduction as well. In the future, we will think about symptoms differently, just by virtue of who is sitting in front of us, and think about preferred treatment methods for women and men very instinctively, as opposed to it only being done at certain centers. I ultimately hope the need for a women's heart clinic will no longer be necessary. That's my very optimistic view. Just like being trained in prevention and intervention, I always thought if I was doing a really good job I'd put myself out of business one way or the other. ■

Dr. Tremmel can be contacted at jtremmel@cvmed.stanford.edu

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