The RIVAL Trial

Timothy A. Sanborn, MD, FACC, FSCAI, and Kimberly A. Skelding, MD, FSCAI, discuss the recently published RIVAL trial data and the potential impact on which access sites operators will utilize for coronary imaging and interventions.


The RIVAL data were presented at the American College of Cardiology's 60th annual scientific session in New Orleans. Full coverage of the data can be found on page 17. To further explore the effect of the RIVAL trial, Cardiac Interventions Today *interviewed Drs. Sanborn and Skelding to get their opinions on these important data.*

What is your immediate take on the data from the RIVAL trial?

Dr. Sanborn: The RIVAL investigators concluded that there was no significant difference between radial and femoral access in terms of the primary outcome of death, myocardial infarction, stroke, and non–coronary artery bypass graft surgery bleeding; both were equally safe and equally effective. There were fewer access site complications (large hematomas and pseudoaneurysms) at 30 days with radial access.

Dr. Skelding: It certainly gives more credence to the radial artery approach because it validated that this approach decreases complication rates—specifically bleeding complications—in a large, prospective fashion. We know that bleeding is associated with mortality, which is an important aspect of using the transradial approach. In addition, radial access had a mortality benefit in ST-elevation myocardial infarction (STEMI) patients, which should be impetus for people to work on their radial skills and improve patient outcomes.

What impact do you think these data will have on percutaneous coronary intervention (PCI) practice in the United States in the short and long term?

Dr. Sanborn: In the United States, we're already seeing attempts to educate and train interventionists in the radial approach. There's quite a bit of data indicating improvement in patient comfort with the radial approach.

In terms of the difference in vascular access site complications, it is important to consider the pharmacology used (bivalirudin vs heparin and glycoprotein IIb/IIIa inhibitors), as well as the access site chosen in these studies. In the meta-analysis comparing radial and femoral access by Jolly et al,[1] bivalirudin was not used in the studies that were analyzed. In the RIVAL trial, glycoprotein IIb/IIIa inhibitors were used in approximately 25% of patients, and fibrinolytic therapy was used in 11% to 12% of patients; bivalirudin was only used in 2% to 3% of patients. It's been shown that heparin and glycoprotein IIb/IIIa inhibitor use are predictors of access site complications.

In the ACUITY trial, the difference in bleeding complications between radial and femoral approaches depended on the pharmacology and not the access site (see *Bleeding Complications Associated With Transradial Versus Transfemoral Access* on page 66). If you look at the patients who were treated with bivalirudin, femoral access site complications were not higher than with radial. When heparin and glycoprotein IIb/IIIa inhibitors were used, radial access did have fewer access site complications than femoral. I did not see an analysis of vascular access site complications with or without bivalirudin, glycoprotein IIb/IIIa inhibitors, or fibrinolytics in the RIVAL data. The pharmacology that was used could be the reason that femoral access had higher access site complication rates than radial access.

Dr. Skelding: Interventionists who have dabbled in transradial access may commit to the approach because they can see a real decrease in complications. In the long term, I think that the number of transradial procedures will continue to increase. We have gone from < 2% to 10% in just a few short years. I suspect that in the long term, there will be much more use of the transradial approach. In addition, I believe that training of the transra-

dial approach will become solidified, and so there will be more formal teaching during fellowships, which is when operators should begin their transradial training.

Should there be another similar trial before practice changes?

Dr. Skelding: As in almost all clinical trials in cardiology to date, < 30% of the patients in the trial were women. Women have a much higher risk of bleeding—particularly elderly women— and therefore that group has the most to gain from this approach. Not all of the questions are answered regarding the transradial approach because the candidates with the most to gain are often passed over in clinical trials. One reason for low enrollment of women is that fewer women undergo invasive procedures in general; we see this in all stent trials, all cardiac pharmacology trials in the catheterization lab, and ultimately, across the board. Importantly, this decreased utility of often lifesaving therapies worsens outcomes for women.

The US Food and Drug Administration and the National Institutes of Health are asking for more data on women, and we should design trials that seek to include an approximate number of women in the study so that we can make meaningful extrapolations of the data, which we haven't done well thus far in the field of cardiology.

Dr. Sanborn: Another trial would require a large number of patients. As the authors of the RIVAL trial point out, a trial of more than 17,000 patients would be necessary to detect a significant difference in the primary outcome. Practice patterns change based on the available literature. There will still be some physicians who are more comfortable with femoral access and will not want to change; there may be a younger generation of interventionists who do want to change. We should be comfortable with both approaches. There may also be an element of patient preference that could have an impact on practice changes.

There are some potential benefits of the radial approach if there is less need for postprocedure monitoring in the catheterization lab; if patients can ambulate in 5 minutes, it might increase your catheterization lab throughput. It certainly increases patient comfort, but there are, of course, benefits and risks to both approaches.

Why do patients who experience a major heart attack gain a significant survival benefit if they are treated radially?

Dr. Skelding: Those are the patients who frequently come in with the most blood thinners on board. Sometimes they come in and they've had thrombolytics, but they've always had an antithrombotic regimen, which often includes glycoprotein IIb/IIIa inhibitors, aspirin, and clopidogrel. Those patients are at the highest risk for bleeding; if we can lower their risk of having an access complication, we can level the playing field. Additionally, there are data in the literature that demonstrate no increase in door-to-balloon times with high-volume radial operators.

Dr. Sanborn: We must be careful of subgroup analyses. The RIVAL trial involved more than 7,000 patients; this included unstable angina, non-STEMI, and STEMI patients. There were fewer than 1,000 STEMI patients in each group (radial and femoral). I would be wary of post hoc subgroup analyses that were not part of a primary endpoint. Furthermore, the various pharmacologic agents used in this trial could have influenced the results in the STEMI patients because 11% to 12% received fibrinolytic therapy, 31% to 34% received glycoprotein IIb/IIIa inhibitors, only 2% to 3% received bivalirudin, and 10% to 11% were not primary PCI patients in which there were probably longer drug infusion times. Remember, bivalirudin was shown to have a mortality benefit compared to the use of heparin and glycoprotein IIb/IIIa inhibitors in the HORIZONS-AMI trial.

How does center volume and the level of operator experience with the radial approach factor into the RIVAL data?

Dr. Sanborn: As physicians gain experience and become more comfortable with the radial approach, their success rates are going to increase, and complication rates will decrease.

Training programs and various national societies are advocating that physicians learn the radial access technique. There is a learning curve, and it does require additional experience and knowledge of different catheters. Not every patient can be treated with the radial approach. In RIVAL, there is a 7.5% crossover rate from radial to femoral, so interventionists should be comfortable with both the radial and the femoral approach. We also have patients with peripheral arterial disease who can't be treated using the femoral approach.

There is an article in *JACC Interventions* in which use of the radial approach increased radiation exposure during diagnostic catheterization procedures.[2] In the RIVAL trial, there was a slight but significantly increased fluoroscopy time with radial as compared to femoral. Other concerns include a lack of good backup guide support with the radial approach as compared to the femoral approach.

Dr. Skelding: High-volume radial operators did better than those who only dabbled in transradial, and they also

did better than the radial operators who were in the predominately femoral centers, which is seen in the trial as a higher crossover rate than normally identified in such studies. The data showed that high-volume radial operators have better outcomes than low-volume radial operators, but there wasn't the same finding with the femoral operators. It wasn't shown that if you went to a high-volume femoral site you had a better result than with a low-volume femoral site.

There have been interviews with operators in the past about the radial approach regarding those who perform it only now and then, and the transradial community is saying, if you're going to be a radialist and are looking for improvement in patient outcomes, that needs to be your consistent approach. There needs to be a transradial-first approach because it's not something that should be done only when absolutely necessary. It should be done every day so that when you must do it, you're fantastic at it.

Dr. Sanborn: High-volume radial centers simply have more experience. If it's a high-volume femoral center, they may have enough radial experience to qualify for participation in the study, but they have more femoral than radial experience overall. Some centers are not dedicated to radial high-volume use, so this could lead toward a higher complication rate.

If the goal of the individual or the center is to develop more radial experience, start with elective and not emergent cases, gain experience with the different guiding catheters and backup support, learn to troubleshoot, and then move toward becoming high volume if the comfort level is there. In the RIVAL trial, interventionists had a requirement of a minimum of 50 radial procedures in the last year, which is low.

How should radial operators who are early in their experience select cases in the STEMI setting?

Dr. Sanborn: If you're going to start your learning experience with radial, I would try more elective cases first to ensure that you have enough experience—at least 100 elective, non-STEMI cases is a good starting point before trying a STEMI case, where the focus is on door-to-balloon times. There have been reports from radial programs that you can have good door-to-balloon times without compromise. I think those results are from operators who have already gained considerable experience with nonemergent cases.

Dr. Skelding: I agree. In addition, they should choose STEMI patients who have a good radial pulse and with whom they don't feel the pressure of getting it right the very first time.

You probably shouldn't start by selecting an 85-year-old woman with STEMI, but instead work with younger patients until you achieve proficiency because we know that when operators begin using the transradial approach, they're a little bit slower with access and in performing the procedure. With highly trained radial operators, there should be no difference in door-to-balloon times between the radial and femoral approach.

How will the Society for Cardiovascular Angiography and Interventions training programs be implemented? Who will be targeted? Is the intention to create more high-volume centers?

Dr. Skelding: The Society for Cardiovascular Angiography and Interventions Transradial Committee runs the transradial training programs. I'm the chair, and Dr. Samir Pancholy is co-chair. We have done three transradial basics programs already, and we have two more coming, which should give physicians the basic didactic information on how to choose their patients, catheters, and approach. We also have simulators at these sessions so that operators can become familiar with the catheter choices and the approach. That's a good place to start. These courses are helpful for those who are just beginning or are in their first few years of learning the transradial approach. We're targeting fellows, those who may be midcareer and who want to change to a transradial approach, and physicians who maybe didn't receive transradial training during their first few years of practice. The programs intend to provide a base on proficiency, but they do not certify people in the transradial approach; they are just an educational forum.

We are now moving toward a higher level of training in the transradial approach, and those programs will follow these initial five. So far, there has been a great interest in these basic programs. We have standing room only at the scientific sessions nationally, and the continuing medical education courses are sold out all year long. So we know that there's a need for these basics, and we're going to continue to offer the basic courses until there is no longer a need for them. However, for those who have already done very well with the transradial basics, we need to offer them a higher-level course so that they can move forward and continue to improve their approach.

As far as creating more high-volume centers, I think that the transradial approach is best performed by operators who use the transradial approach as their default—transradial first—and then move to femoral if there's failure.

We want to create more high-volume centers with physicians who are using transradial as their initial approach because there's been so many data out there regarding the importance of lowering access-related bleeding complica-

tions, and if we take this on as a field, we can really make a huge impact on patient outcomes.

Dr. Sanborn: There's a big difference in terms of interventional centers across the country. There are many hospitals that may be serving rural areas where there will never be high volume. There are also metropolitan areas such as Chicago where there are numerous interventional programs, so they too may not have the high volume that we see in other areas.

What concerns should be elucidated regarding the trial itself?

Dr. Sanborn: As I mentioned before, the various pharmacologic agents used in this trial (fibrinolytics, glycoprotein IIb/IIIa inhibitors, and low bivalirudin use), as well as the 10% to 11% non–primary PCI STEMI cases in which there was probably a long drug infusion time, may have influenced the results. Also, vascular closure devices were only used in 25% of the femoral cases in the RIVAL trial. In our review of bleeding complications associated with radial and femoral access (see page 66), we reported on several studies showing reduced access site complications with the combination of vascular closure devices and bivalirudin.

Dr. Skelding: My concern about the approach is that you can't be a successful femoral operator and assume you can turn to transradial every now and then and be equally as good at the transradial approach. That said, you can become very good at the transradial approach by dedicating some time and some cases to doing it; in fact, your backup support, particularly for the right coronary artery, is superior. But you must be patient. In your first few cases, you might take a little bit longer, so you need to be ready for that. It's probably not best to start the transradial approach on your busiest cath lab when you've got 15 patients to see in the afternoon. However, with time and dedication, you can excel at the approach and improve patient outcomes. Patients prefer the transradial approach on a comfort level and a convenience level, but really, we need to improve our bleeding rates and improve mortality.

My concern about the RIVAL trial is that people will only read the headline and see that there isn't any difference between the femoral approach and the radial approach in the primary outcome in all comers, and they won't read the rest of the information, which I think is vitally important. We can make a real difference in the STEMI population. We should work to become proficient at the elective transradial approach so we can show its benefit in STEMI patients, and vascular access complications can be significantly decreased by changing techniques. There are few other areas in the cardiology field where we can make such a big difference with just a change in technique, and I think that's the important part of the RIVAL trial. Some physicians simply are not going to read past the headlines to the important points therein. I think that this is just the beginning of the data and outcome information that we're going to see on the transradial approach.

What are your take-home points about the RIVAL trial?

Dr. Sanborn: I would encourage interventionists to attend a course on radial access to become more knowledgeable about the procedure overall. There are cases that can't be performed via femoral access and therefore must be done radially. If you choose to stick with femoral, make sure you do it as safely as possible. Consider the use of vascular closure devices and a direct thrombin inhibitor such as bivalirudin.

Dr. Skelding: We have a real ability to make a difference in morbidity and mortality rates in the STEMI population if the transradial approach is adopted. But importantly, all patients have a decreased bleeding risk with this approach. We need more data on populations such as women and the elderly who have the highest bleeding risks. There is a learning curve, but it can be overcome with more experience. If you are serious about the transradial approach, it should be your default strategy so that your skills are consistently being utilized, as this is the group of operators who seem to demonstrate the highest benefit for patients. ■

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1. Jolly SS, Amlani S, Hamon M, et al. Radial versus femoral access for coronary angiography or intervention and the impact on major bleeding and ischemic events: a systematic review and meta-analysis of randomized trials. Am Heart J. 2009;157:132-140.
2. Mercuri M, Mehta S, Xie C, et al. Radial artery access as a predictor of increased radiation exposure during a diagnostic cardiac catheterization procedure. JACC Cardiovasc Interv. 2011;4:347-352.