

Lessons Learned in RESILIENT

Co-Principal Investigator John R. Laird Jr, MD, discusses the results and impact of this landmark SFA stenting trial.



What are the goals of the RESILIENT trial?

At the time the trial began, there was still controversy over whether stents improved outcomes in the superficial femoral artery (SFA). There were certainly some early trials with negative results, and there have been conflicting data recently, including results from the ABSOLUTE study from Vienna, which demonstrated a beneficial effect from stenting compared to balloon angioplasty, and the FAST trial, which showed no clear benefit. The goals of the RESILIENT trial were to provide additional information about the potential benefits of nitinol stents versus balloon angioplasty in the SFA and to test a new, flexible, fracture-resistant nitinol stent in this vascular bed.

What were the lesion lengths and patient criteria included in phase 2 of the trial?

Lesions up to 15 cm in length could be treated. The lesion lengths in RESILIENT ended up being shorter than what we have seen in some of the other recent SFA stenting trials. The mean lesion length in the stent group was approximately 6.2 cm. The mean lesion length in the balloon group was 5.7 cm. However, one of the important design features of the trial was that more than one SFA lesion could be treated, as long as the total lesion length did not exceed 15 cm. As a result, the total mean treated lesion length per patient in the stent group was about 7 cm, versus 6.4 cm in the angioplasty group.

Patients were included in the trial if they had intermittent claudication or ischemic rest pain. The lesions had to be confined to the SFA and/or proximal portion of the popliteal artery. In addition to the noninvasive

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vascular testing, quality of life was assessed pre- and postintervention with the walking impairment questionnaire.

How do the results of RESILIENT compare with those of other major stenting trials?

The patency data from the RESILIENT trial are excellent. At 1 year, the primary patency by duplex ultrasound was just under 80%, which compares very favorably with all of the other trials. The stent fracture rate was low, indicating that this stent is perhaps less prone to fracture than some of the first-generation nitinol stents. In fact, the RESILIENT fracture rate was lower than that seen in the DURABILITY 1 trial.

However, it is clear from both of these trials that when these very flexible stents are stretched during deployment, they are more prone to fractures. Technique is very important during the deployment of these stents; if the delivery is executed properly, then the incidence of fracture should be very low for both the LifeStent (Bard Peripheral Vascular, Tempe, AZ) and the Protégé EverFlex stent (ev3, Inc., Minneapolis, MN).

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patency. In ABSOLUTE and the more recent DURABILITY study, lesion lengths were longer, in the 9- to 12-cm range, and the 6- and 12-month primary patency rates were lower than what was seen in the RESILIENT trial, which had shorter lesion lengths.

I also think that the advantage of stenting over balloon angioplasty increases with increasing lesion length. None of the previous trials, such as FAST and Intracoil, in which short lesions were studied, were able to show a benefit of stenting over angioplasty. RESILIENT, ABSOLUTE, and DURABILITY have shown that when longer lesions are treated, the advantage of stenting is greater.

How significant are the roles of delivery system technology and operator technique in the incidence of stent fracture?

Evolving delivery system technologies also play a role; the delivery system used in the beginning of the RESILIENT trial was the first-generation LifeStent NT delivery system, and it was not the optimal technology. With this delivery system, it was easier to inadvertently compress or stretch the stent during deployment. Much of that has been remedied with the second-generation FlexStar delivery system design.

In terms of technique, it is very important when deploying these stents not to rush. After the distal portion of the stent has been expanded and is attached to the vessel wall, the focus needs to shift to the proximal marker, ensuring that it neither advances nor pulls back during the remainder of the deployment, which will prevent stretching or compression of the stent. It is also clearly important not to attempt to stretch the stent to cover a lesion when the stent length is slightly shorter than the length of the lesion to be treated. It is better to add an additional stent rather than risk elongation of the first stent, which can increase the risk of stent fracture.

Previous SFA stenting trials have seen increased incidences of stent fracture and lower patency rates as they reach 2-year follow-up versus their 1-year data. How do you anticipate the RESILIENT 2-year data will fare in this regard?

We are eagerly awaiting the 2-year RESILIENT data to answer that very important question. Virtually all of the previous SFA stenting trials have shown some late restenosis between 1 and 2 years, so some continuation of this trend may be inevitable. Hopefully, these more flexible stent designs will have lower incidences of late restenosis. At least theoretically, there will be less chronic injury occurring in the vessel with a more flexible, kink-resistant endoprosthesis.

In your opinion, do the RESILIENT data show sufficient safety and efficacy for FDA clearance of the LifeStent for use in SFA and proximal popliteal lesions?

Absolutely. There were no safety issues whatsoever with regard to the LifeStent; there were no significant early major adverse cardiac events or problems in the periprocedural period. The 1-year patency data were excellent, the fracture rate was low, and many of the serious fractures could be attributed to technique issues during deployment. Even when fractures occurred, at least in this study, they were not associated with restenosis or the need for target vessel revascularization. In my opinion, the data are very strong, and they support approval for this device in the SFA and proximal popliteal artery.

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What is the exact indication you think it should have?

I think we have determined in the RESILIENT study that lesions up to 15 cm long can be treated with stents and achieve better results than with balloon angioplasty. What we do not yet know is whether stents will provide good results when used for longer lesions, in the 20- to 30-cm range. We also do not know if stenting will provide the best option in the popliteal artery beyond the proximal third, and certainly we must be careful in using these stents in other vasculature, such as the iliac and common femoral arteries, which we did not evaluate in this trial.

Based on some trials studying carotid artery stenting, many people strongly believe that there is a significant influence of operator experience on outcome. To what degree do you think this is a factor in the SFA?

I think operator experience is a much less significant issue in the SFA than in the carotid arteries. The downside to minor mistakes or a lack of optimal technique in the carotid anatomy is dramatically greater than it is in the SFA. Clearly there are some technique issues with regard to SFA stent deployment (some of which have already been discussed); for instance, it is important to stent the entire lesion and also to not dilate outside of the stent with the balloon to avoid edge effect or restenosis outside of the stented segment. But overall,

the technical difficulty associated with this procedure is dramatically different from that of carotid stenting, and the learning curve is not nearly as steep.

Do you think real-world or postapproval outcomes will approximate those observed in the RESILIENT trial setting?

Yes, as long as the stent is used in lesion subsets similar to those included in these trials.

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As you mentioned, part of the reason RESILIENT has shown better results than previous trials is that it involved the use of a second-generation nitinol stent. To what degree do you think current stent designs can still be improved upon, thereby improving outcomes as well?

I think there is room for slight improvement with regard to the device itself. None of these stents have been shown to be perfect in terms of their resistance to fracture. There may be ways to tweak the manufacturing process and ways to improve the stent surface preparation/polishing to increase the durability of the stent. There is room for improvement in the delivery systems as well, to make it tougher to compress or elongate the stents. But ultimately, I think we will reach the limit on what can be achieved with the stent itself. Any significant improvement beyond that will require coatings or perhaps drug delivery to impact on the longer-term results.

What can RESILIENT tell us about the efficacy of PTA in SFA therapy?

Over the past few years, we have learned that balloon angioplasty is a reasonable option for short SFA lesions, <4 cm in length. However, if PTA is used for longer lesions, the results are quite poor. In the RESILIENT trial, there was a significant need for bailout stenting because of suboptimal angioplasty results. Stenting was required in 40% of cases due to major flow-limiting dissections or residual stenosis >30%. When we broke down the data on the patients who did cross over, most of them had longer and more calcified lesions than those patients who did not require bailout stenting. The 12-

month patency data from RESILIENT's balloon angioplasty arm are similar to what was seen in the VIVA Physicians, Inc. Objective Performance Criteria.

How has what you have learned as principal investigator of RESILIENT impacted your own everyday practice?

I came away from this trial with a more favorable view of SFA stenting using the second-generation, more flexible nitinol stents. The results of RESILIENT have caused me to lower my threshold for stenting, although I realize that we still have a lot more to learn about SFA stenting, including what the longer-term results are.

Another trial for which you will serve as principal investigator has received conditional IDE approval to begin from the FDA. What can you tell us about this trial?

In the near future, we should be starting an SFA stenting trial using the Complete SE stent (Medtronic Vascular, Santa Rosa, CA), and I will serve as the national principal investigator. My initial impression is that this is an excellent stent, with good characteristics for the SFA. The trial will include longer stents, up to 15 cm in length, treating disease in the SFA and proximal popliteal arteries, so we will have another opportunity to learn more about stenting in this vascular territory. This will be a single-arm trial. At this point, I think we have learned enough about balloon angioplasty in the SFA that we no longer need to randomize against a PTA control arm. ■

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