AN INTERVIEW WITH...

Janet T. Powell, MD, PhD, FRCPath

Prof. Powell discusses her work as a trial investigator, including what the latest EVAR data show and areas that warrant further study.

As one of the lead investigators in numerous landmark trials, including EVAR 1, EVAR 2, and IMPROVE, how has your work as a trialist shaped your daily efforts as a clinician?

Patients have different attitudes and values compared to clinicians, and it is very important to listen to and respect their values. My work as a trialist means that I am willing to spend time on guideline panels and argue that patients need to be involved in developing guidelines—at the moment, they are not and this is wrong.

What was the finding or data point that most surprised you in the recently presented and published 15-year follow-up data from EVAR 1?

The fact that about one-quarter of these patients survive for 15 years and beyond, which underscores the need for a durable repair of large abdominal aortic aneurysms. We need to think of any repair being durable for about 20 years.

What is your hypothesis on the cause of the increased cancer mortality outcome observed in the endovascular aneurysm repair (EVAR) group of the EVAR 1 trial? Do you believe that this should be further explored, and if so, by what means?

This was one of my original hypotheses when we planned the very long-term follow-up of EVAR 1, but not a hypothesis that found strong support among my colleagues. The strongest candidates for increased cancer mortality would be those who have had increased exposure to radiation during treatment, follow-up, surveillance, and reinterventions. The EVAR 1 results have provided support for my initial hypothesis that the additional radiation burden associated with EVAR would result in a higher incidence of later cancer diagnosis and associated cancer deaths. This very concern has supported the switch from CT to duplex ultrasonography for surveillance, so obtaining new, good-quality data to support this hypothesis may prove very difficult. However, valuable information might be gleaned from registry and administrative databases (eg, Medicare, linking Swedvasc with the Swedish cancer registry).

Based on the findings of the trials in which you have participated, which are the most critical factors that distinguish a good EVAR candidate from a patient better suited for surgery?

All patients with appropriate aortic morphology are potential EVAR candidates, and the risks of both open repair and EVAR need to be discussed frankly and honestly with them, and then the patient should decide. Do they want to trade the benefit of lower operative mortality from EVAR with the possibility that they will need lifelong surveillance and reinterventions, or do they prefer to take the mortality hit early and get discharged as an aneurysm patient within a year? This will vary from patient to patient, and the decision should belong to them. There are some indications from our individual patient data meta-analysis of the trials on EVAR versus open repair that at least over the first 5 years, it is the fittest patients who gain most survival benefit from EVAR, as catch-up mortality is faster in patients of marginal fitness.

If you were awarded a grant providing sufficient funding of a randomized aortic aneurysm trial to begin in 2018, what would you seek to study? What would be the essentials of the design, population, included therapies, and follow-up protocols?

Only one trial? I am probably best placed to further improve the management of rupture, where there

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are several unanswered questions including whether early administration of transexamic acid or the use of locoregional versus general anesthesia would save lives. However, the trial I am involved in planning is on the use of metformin in patients with small aneurysms, where the primary outcome will be aneurysm growth rate, and the secondary outcome will be cardiovascular events (metformin is hypothesized to reduce both of these outcomes). However, the key may be starting metformin early enough in the development of an abdominal aortic aneurysm (AAA), perhaps at aortic diameters of 2.5 to 3 cm. The methodology will be rather similar to that used in the AARDVARK trial, but with better quality control of the measurement of AAA diameter and with many more patients.

What is your take on the recently reported data showing that familial AAA predicts a higher 30-day mortality rate after EVAR, and how might this information contribute to our current knowledge and affect treatment decisions?

This study is thought provoking but subject to many potential confounders, particularly the label of familial AAA (women are better historians than men and are known to have higher operative mortality), the presence of occult coronary artery disease, and lifestyle factors (including smoking) in these patients.

What steps need to be undertaken to improve AAA care in women? What data are currently most critically needed, and what can be done by vascular physicians in the short term to ensure the best possible care in their female patients?

Beware, I could write far too much on this topic! First, we need to consider whether we need sex-specific definitions for aneurysms in women, given that, in general, they have smaller-diameter arteries than men. Looking at the normal distribution of aortic diameters in older women, I would suggest that an infrarenal aortic diameter of 2.5 cm (more than three standard deviations above the mean) might be considered a small aneurysm in women. This would have the knock-on effect of indicating that the threshold for intervention should be about a 5-cm diameter. We also need to understand why operative mortality from both EVAR and open repair is so much higher in women than men. This sex difference in operative mortality may not be unique to AAA repair and has been observed for coronary artery bypass surgery and resection of colon cancer. Talk to surgeons and they say, "I know, but women are higher risk than men." My response is that is merely an excuse for not finding out why, and perhaps we do not fully understand the physiology of older women. This needs to be better understood, so that procedures, such as anesthesia, fluid or blood replacement, and pain management, might be tailored differently for men and women.

In 2012, you were recognized for your "Dedication to Creating Consensus Within the Medical Community." At what point in your career did striving for consensus become paramount? Did any observation or event focus your efforts in this direction?

I was surprised and highly delighted by this recognition. Consensus should be reached by opening eyes to all the available evidence and level of available technology and expertise, as well as being cognizant of the different health economies from which the evidence is derived. I guess that I have never been afraid to speak out, even when I knew the information I was giving would be unpopular (eg, the result of the EVAR 2 trial). Perhaps this is why I was selected for this recognition.

What would your colleagues in the vascular community be most surprised to learn about you?

I grow all my own vegetables, some of them in the greenhouse. ■

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