Virginia D. Steen, MD: Pushing the Envelope of Research, Redefining the Link Between Scleroderma and PAH

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For Virginia D. Steen, MD, the journey essentially began at the University of Pittsburgh in the 1980s where she was a Fellowship in Rheumatology and began to see her first patients with scleroderma and an "isolated" pulmonary hypertension independent of pulmonary fibrosis. In this era before any treatments were approved, before the landmark studies that would revolutionize the treatment of the disease, rheumatologists remained on the fringes of PH research. Although rheumatologists generally do not participate in the clinical trials in PH, largely because of the relatively smaller number of patients in their care who can be evaluated, efforts by Dr Steen and her colleagues over more than 20 years have helped research the connection between scleroderma and pulmonary arterial hypertension. This has led to a tremendously improved understanding of the natural history of PH in scleroderma, the risk factors for predicting PH in patients with this coexisting disease, and the response to the newer therapies approved within the last 5 to 6 years.

The initial work, however, and the impetus for extending her study of PH in scleroderma, began with Dr Steen's first paper on the natural history of the association. "After the initial observation of PH occurring in scleroderma, we looked at 30 patients who had PH and scleroderma and compared them to similar scleroderma patients who did not have PH," recalled Dr. Steen. This study showed patients with PH in scleroderma did not have significant fibrosis but had a very low diffusing capacity. Some had this finding prior to the diagnosis of PH. "In our next study, using the Pittsburgh Scleroderma Database, our prospective collected database, we performed a retrospective case control analyses, looking at pulmonary function and echo[cardiogram]s prior to the diagnosis. The pulmonary function tests showed that even 5 years before their diagnosis their DLCO [diffusing capacity of the lung for carbon monoxide] was decreased."

Dr Steen and colleagues have published more than 50 articles and editorials that form the core of the most extensive database of articles in this clinical setting. Studies that addressed topics such as predictors of end stage lung disease in systemic sclerosis and other findings that contributed to the evidence-based clinical practice guidelines of the American College of Chest Physicians. In these and ensuing years, she became Professor of Medicine at the University of Pittsburgh and then, in 1995, moved to her current position as Professor of Medicine at Georgetown University, Washington DC, where she also serves as Program Director of the Rheumatology Fellowship Program.

As their research progressed, Dr Steen and her team began to identify features of scleroderma patients that helped differentiate subsets within the overall category. "There are those typical PAH [pulmonary arterial hypertension] patients who look—other than their age and having scleroderma—very similar to idiopathic PAH patients. But then there is another group of scleroderma patients who have more interstitial disease with their PH. And there is a group who have more heart disease but still have vascular pulmonary hypertension. The recognition of these different groups has evolved as more treatments have become available."

The focus of much of her current research centers around the PHAROS: Pulmonary Hypertension Assessment and Recognition of Outcomes in Scleroderma. This is a multicenter, 18-site study of systemic scleroderma (systemic sclerosis) patients in the United States who are at high risk for developing pulmonary hypertension as well as those with newly diagnosed pulmonary hypertension. This is an extremely important study since pulmonary hypertension is the most common cause of scleroderma deaths. It is looking specifically at patients who are at high risk for PAH, those who have specific abnormalities on pulmonary function tests (PFTs) or echocardiograms as well as those who are newly diagnosed with PAH.

"We have close to 300 patients now and almost a third of them have definite PH," said Dr Steen. "We are following these patients' response to therapy to determine their outcome. We are also following patients who are at high risk for PH over 5 years to determine who develops PH based on various risk factors. For example, I am doing an exercise study and we've shown that if a scleroderma patients is at high risk he or she has a 40% chance of having exercise-induced PH even if one has resting normal pressures."

The findings coming from the rheumatology community are an essential component in the expanding translational research that Dr Steen and her colleagues hope will enable clinicians to identify risk factors much earlier in scleroderma and initiate preventive therapy at a stage that can make a real difference in altering the natural history of the disease. ■