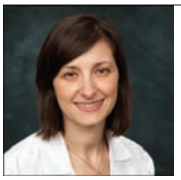
Review of the Latest Published Research



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Summaries and commentaries from the section editors and invited reviewers present a clinical context for practitioners' application of the latest published research relevant to the care of patients with pulmonary hypertension. In this issue, Ioana Preston discusses a study of chronic anticoagulation therapy in PAH patients.

Johnson SR, Granton JT, Tomlinson GA, et al, **Warfarin in systemic sclerosis-associated and Idiopathic Pulmonary Arterial Hypertension. A Bayesian approach to evaluating treatment for uncommon disease. J Rheumatol 2012; 39;276-285**

The role of chronic thrombosis in pulmonary arterial hypertension (PAH) is controversial.[1,2] It is not clear whether the thrombotic arteriopathy previously described in pathology samples from PAH patients are an epiphenomenon or an integral part of the pulmonary vascular remodeling. The experience with anticoagulation is derived from one retrospective cohort and two prospective studies that showed that the use of warfarin was associated with better outcome in PAH.[2-4] These studies looked only at patients with idiopathic PAH (IPAH), heritable PAH, and PAH due to anorexigen use. To date, there are no prospective studies on the effects of anticoagulation in other forms of PAH.

A recent study by Johnson et al proposed to evaluate the effect of warfarin on survival in patients with PAH associated with scleroderma (SSc-PAH) and IPAH.[5] Using a novel approach (Bayesian), authors queried the largest two longitudinal PAH cohorts in Canada. Patients were included if they had one of the two types of PAH, as defined by current guidelines. The exposure was treatment with warfarin at any time after diagnosis of PAH, without specifying a minimum duration, and the primary outcome was time from diagnosis of PAH to death from all causes. After reviewing 1138 charts, the IPAH and SSc-PAH groups were matched to baseline severity of disease and exposure to PAH-specific therapies. In the matched cohorts, 98 patients were identified with SSc-PAH;among those, 49 were treated with warfarin. Among the 66 patients with IPAH identified, 33 were on warfarin. The 3-year survival in the SSc-PAH cohort was 61% for the warfarin-unexposed patients and 58% for the warfarin-exposed patients. The 3-year survival in the matched IPAH cohort was 83% for both the warfarin-unexposed and exposed patients. Taking into account the predicted survival with a median of 4.9 years in the untreated patients with SSc-PAH, the probability of improving survival by 6 months or more with warfarin was 23.5%. For clarification, a 50% probability of improved survival translates into merely a flip of the coin. Similarly, for the IPAH group who was given a predicted median survival of 3.9 years if left untreated, the probability of improving survival by 6 months or more with warfarin was 27.7%.

These results translate into a low probability that warfarin improves survival in both SSc-PAH and IPAH. Another interesting observation derived from this analysis was that patients with both SSc-PAH and those with IPAH who have been exposed to warfarin had worse functional class, more right ventricular dysfunction, and use more PAH medications than unexposed patients. This suggests a bias from the treating physicians to using anticoagulation therapy in more advanced disease.

Additionally, the analysis provided insight into potential side effects of chronic anticoagulation. In SSc-PAH patients who have gastrointestinal vascular lesions and are at theoretical risk for increased gastrointestinal bleeding while anticoagulated, warfarin use did not increase the risk of hemorrhagic stroke or gastrointestinal bleeding requiring transfusion in this subgroup. In the IPAH group, gastrointestinal bleeding occurred in 2% of the warfarin-unexposed and 7% of the warfarin-exposed patients and hemorrhagic stroke occurred in one warfarin-unexposed patient with IPAH.

While authors acknowledged potential limitations, especially the presence of potential confounders and the small sample studied, this study using an innovative methodological approach to published literature suggested that, in the era of PAH-specific therapies, the use of anticoagulation in both IPAH and SSc-PAH warrants further research.

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References

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