Venous Thromboembolism in Systemic Sclerosis: Prevalence, Risk Factors and Effect on Survival

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www.youtube.com/watch?v=XgGJyGQ2v4E&t=11s

Venous thromboembolism is a vascular phenomenon that's associated with the development of either deep vein thrombosis or pulmonary embolism. This is common in the general population and can be seen in people with systemic sclerosis. As a consequence, when a patient presents to clinic with either a DVT or PE in the setting of systemic sclerosis, they will often ask, "Is this related to my disease?" When we think about biologic plausibility, it is conceivable that it is related to systemic inflammation. We know that active systemic inflammation is associated with increased TNF-α levels as well as endothelial activation. Together this can lead to increase in tissue factor, decreased protein C and platelet activation, together leading to a procoagulable state.

A recent metaanalysis of systemic rheumatic diseases and its association with vascular thrombotic embolism found that there was an increased risk of VTE events in patients with systemic inflammatory disease. However, when you look at the subgroups, namely systemic sclerosis, there were only 4 studies evaluating the development of VTE in patients with systemic sclerosis. This led our group, led by our fellow Nabil Hakami, to evaluate the prevalence and incidence of venous thromboembolism in systemic sclerosis, to evaluate risk factors and its impact on survival.

We conducted a retrospective cohort study with primary data collection of patients who fulfill the ACR-EULAR classification criteria for systemic sclerosis. Patients with localized system sclerosis, overlap syndromes, and undifferentiated connective tissue disease were disqualified from this study. The study period was 1970–2017. Deep vein thrombosis was defined as the presence of thrombus in the extremity, femoral, or popliteal veins with extension proximally on Doppler ultrasound. The presence of pulmonary embolism was defined as the presence of emboli on CT thorax angiogram. CT ultrasound and CT scan were also performed based on clinical suspicion. In our study, we evaluated 1181 subjects, of whom 3.4% developed a venous thromboembolic event, 1.7% developed a deep vein thrombosis, and 2.2% developed pulmonary embolism. This gave a cumulative incidence of 2.7% per 1000 patient-years. We found that compared to a general population prevalence of VTE of 2 cases per 1000 person-years, the prevalence of VTE in systemic sclerosis was not different than the general population, that is, it was not statistically significantly different.

When we looked at subgroups, we found a number of interesting hypothesis-generating findings. First, among patients with systemic sclerosis–associated interstitial lung disease, the frequency of deep vein thrombosis was higher as well as the frequency of pulmonary embolism. Furthermore, we found that there was no significant difference in the occurrence of DVT or PE between systemic sclerosis patients with the limited or diffused subtypes. When we looked at survival, we found an unadjusted hazard ratio of 1.16, and similarly the adjusted hazard ratio was 1.02, suggesting there was no significant difference in survival between systemic sclerosis patients with and without venous thromboembolic events.

So in conclusion, we found that the risk of venous thromboembolic events in systemic sclerosis is comparable to the general population. That is, VTE is not independently associated with survival in

systemic sclerosis. The presence of pulmonary hypertension, peripheral arterial disease, and ScL70 antibodies, and anticardiolipin antibodies are risk factors for the development of venous thromboembolism. If you would like to read further about this body of work, and our findings, I encourage you to please look at *The Journal*'s website for the full manuscript.

Thank you.