Assessment of arterial damage in vascular Ehlers-Danlos syndrome: a retrospective multicentric cohort


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Background: Vascular Ehlers-Danlos syndrome (vEDS) is a rare inherited connective tissue disorder due to pathogenic variants in the COL3A1 gene, leading to medium-size artery (MSA) dissection, aneurysm, and rupture with a poor prognosis. Conversely, aortic lesions are rarer and less investigated.

Purpose: To describe the association between the distribution of MSA and aortic lesions and the type of COL3A1 variants in a multicentric cohort of vEDS patients.

Methods: Analysis of the 330 vEDS adult patients from the French RaDiCO SEDVASC registry. At the time of the study, 87% were alive, 60.3% were index cases and 60.0% females. Median age at molecular diagnosis was 36 years (IQR 24.3–46.8). COL3A1 variants were identified using NGS and/or Sanger sequencing and classified according to their functional consequences: 80.6% dominant-negative (DN) and 19.4% leading to haplo-insufficiency (HI). Computed tomography angiography (CTA) was systematically performed during the initial work-up of patients. Carotid mechanics was also assessed by echotracking in a subgroup of 133 patients.

Results: Arterial lesion history was reported in 82.4% of the patients (N=272), with 227/272 patients (83.5%) having MSA lesions alone, 9 (3.3%) aortic lesions alone and 36 (13.2%) both. DN variant was associated with higher prevalence of arterial lesions than HI variant (P 0.044), especially on supra-aortic trunks and renal arteries (P 0.018 and P 0.0003 respectively). Importantly, the higher prevalence of aortic lesions observed in HI patients with arterial lesions versus DN patients (P 0.027) was not significantly different when adjusted for age (P 0.559). Carotid Young’s modulus was lower in DN than HI patients (P 0.014), in association with the higher incidence of MSA lesions in this genotype group.

Conclusion: The prevalence of aortic lesions is not influenced by the COL3A1 genotype when adjusted for age. vEDS patients with DN variants have a higher frequency of MSA lesions especially in supra-aortic trunks which is associated with a lower carotid stiffness, suggesting a need for an optimal care for this subgroup of patients.