Aortic and arterial manifestations and clinical features in TGFB3-related heritable thoracic aortic disease: results from the Montalcino Aortic Consortium

BACKGROUND: Pathogenic variants in TGFB3 may lead to a syndromic genetic aortopathy. Heritable thoracic aortic disease (HTAD) and arterial events may occur in TGFB3-related disease but there are limited outcomes data on vascular events in this condition.

METHODS: Clinical data, phenotypical features and aortic outcomes in individuals with pathogenic/likely pathogenic (P/LP) TGFB3 variants enrolled in the Montalcino Aortic Consortium registry were reviewed.

RESULTS: 34 individuals (56% male, median age 42 years, IQR 17-49, range 3-74 years) with P/LP TGFB3 variants were studied. Craniofacial, cutaneous and musculoskeletal features seen in Loeys-Dietz syndrome were variably present. Extra-aortic cardiovascular features included arterial tortuosity (25%), extra-aortic arterial aneurysms (6%) and mitral valve prolapse (21%).Aortic dilation (Z-Score>2) was present in 10 individuals (29%) and aortic dissection occurred in 2 (6%). Type A aortic dissection occurred in two patients (aged between 55 years and 60 years), and one of these patients experienced a type B aortic dissection 6 years later. Seven adults (median age 62 years, range 32-69 years) with aortic root dilation (41-49 mm) are being followed. No patients have undergone prophylactic aortic surgery. Twenty-five per cent of children have aortic dilation. Sixty-eight per cent of the entire cohort remains free of aortic disease. No deaths have occurred.

CONCLUSIONS: TGFB3-related HTAD is characterised by late-onset and less penetrant thoracic aortic and arterial disease compared with other transforming growth factor β HTAD. Based on our data, a larger aortic size threshold for prophylactic aortic surgery is appropriate in patients with TGFB3-related HTAD compared with HTAD due to TGFBR1 or TGFBR2 variants.