# What the Vascular Surgeon Needs to Know about Ehlers-Danlos Syndrome Based on the Mayo Clinic Experience

*Jean M. Panneton, MD, Norfolk, VA*

Ehlers-Danlos syndrome (EDS) encompasses a variety of types of inherited connective tissue disorders. Although most patients have the classic form with joint hypermobility, increased skin elasticity, and tissue fragility, EDS comprises a heterogeneous group of clinical syndromes with distinct inheritance, biochemical defect, and prognostic implications. EDS type IV (EDS-IV), the vascular or arterial-ecchymotic type, is a rare autosomal dominant disorder resulting from mutations in the gene encoding for type III procollagen (COL3A1) synthesis. Different from the other forms, EDS-IV may lead to premature death from spontaneous arterial, intestinal, or uterine rupture. Patients are typically unaware of the diagnosis until they present, often to a vascular surgeon, with an arterial complication. Management is challenging because of extreme tissue fragility, and numerous reports emphasize the exceedingly high risk of massive bleeding and anastomotic disruption with attempted operative repair. The purpose of this presentation is to review the spectrum, management and clinical outcome of EDS-IV patients.

Using the vascular surgery and medical genetics registries, we identified 31 patients with EDS-IV who were evaluated at the Mayo Clinic between January 1, 1971, and January 1, 2001. Clinical diagnosis was made on the basis of at least two of four major diagnostic criteria, as defined by the revised nosology of Villefranche, 1997: thin, translucent skin, extensive bruising, characteristic facial features, and history of arterial, intestinal or uterine fragility. Patients with other connective tissue dysplasias were excluded. We attempted to ascertain whether the complication and/or cause of death were associated with EDS-IV or not. Vascular complication was defined as arterial or venous rupture, dissection, aneurysm formation, and organ rupture.

Twenty-four patients (77%) had biochemical confirmation of abnormal procollagen III synthesis, 11 patients had COL3A1 gene mutation, and 7 patients were diagnosed solely on the basis of clinical criteria. The mean age at time of diagnosis was 28.5 ± 11 years (range, 10-53 years). Nonvascular complications occurred in 20 patients (65%). Twenty-four patients developed 132 vascular complications. Of the 132 complications, 63 were symptomatic, 69 were incidental imaging findings, 78 were present prior to or at time of initial evaluation, and 47 de novo complications occurred during a median follow-up of 6.3 years. Survival free of vascular complications was 90% at 20 years, 39% at 40 years, and 20% at 60 years of age. Most problems consisted of arterial dissections/dissecting aneurysms (n = 57, 48%) or arterial ruptures with or without contained hematomas (n = 45, 38%). True fusiform aneurysms occurred in a minority of cases (n = 17, 14%). Fifteen patients underwent 30 operative or interventional procedures. The majority of these procedures (70%) were performed in an emergent or urgent basis. Indications were arterial rupture with active bleeding in 14 cases (47%), large aneurysm size in 10 (33%), and rapid aneurysm expansion in 2. Procedures included arterial reconstruction (15), simple repair or ligation (4), coil embolization (3), splenectomy (2), and abdominal decompression, nephrectomy, graft thrombectomy, vein stripping, and thoracoscopy (1 each). There were 3 hospital deaths from exsanguinating hemorrhage, 2 of them following operative interventions and 1 due to ruptured splenic artery. Early procedure-related morbidity was 46%, including 37% incidence of postoperative bleeding. The incidence of late graft-related complications was 40%, including 4 anastomotic aneurysms, 1 fatal anastomotic disruption, and 1 graft thrombosis. Patient survival was 68% at 50 years and 35% at 80 years of age. Eleven of the 12 deaths during the study period were associated with EDS-IV related arterial ruptures.

There is currently no effective medical treatment that can predictably decrease the risk of vascular complications and increase life expectancy in patients with EDS-IV. However, the diagnosis should be considered in young patients with unexplained vascular complications, particularly if there is a family history for vascular, intestinal, or uterine rupture. Invasive imaging studies should be avoided whenever possible and computed tomography (CT) or magnetic resonance angiography provide excellent means of evaluating the extent of complications. Operative treatment is indicated in patients with frank or imminent life-threatening bleeding. Although operative mortality was not excessively high in this study, the incidence of postoperative bleeding complications and late graft-related problems was significant. In addition, despite successful repair of vascular complications, survival was shortened owing to secondary vascular or graft-related complications.

**References**

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