Introduction: Ehlers-Danlos syndrome (EDS) is a heterogenous group of autosomally inherited connective tissue disorders characterized by skin fragility and joint hypermobility. The primary defects surround the synthesis and structure of fibrillary collagen. There are multiple subtypes of this disease secondary to numerous genetic mutations including classical, hypermobility, vascular and others. Ehlers Danlos syndrome has a prevalence of one in every 25,000 births. Type IV, the vascular subtype, accounts for 4% of Ehlers Danlos patients and is the only subtype associated with increased mortality secondary to spontaneous arterial aneurysm and dissection in addition to uterine or intestinal rupture. In fact 25% of individuals with vascular Ehlers Danlos Syndrome experience a major complication by age 20 and more than 80% by age 40. The median lifespan in this subtype is just 50 years of age. It is characterized by a mutation in the COL3A1 gene leading to a structural defect in the pro1(III) chain of type III collagen. Detailed below is a report of a challenging night shift with simultaneous presentation of two patients with different manifestations of Ehlers-Danlos syndrome with a discussion of the anesthetic implications.

Cases: A 25 year old female presented with abdominal pain with subsequent CT scan indicating perforated viscous with associated pneumoperitoneum. Her past medical history was significant for Ehlers Danlos syndrome Type IV and an associated history of easy bruising and bleeding from minimal trauma. The patient was scheduled for laparoscopic abdominal exploration which subsequently converted to open with sigmoidectomy and end descending colostomy. She arrived to the operating room in stable condition; therefore arterial line placement was avoided given her likely friable vasculature and risk of hematoma and dissection. Considering her history of easy bruising and bleeding, she was prophylactically given a 0.3 mg/kg dose of desmopressin to prevent coagulopathy. Thromboelastogaphy (TEG) performed intraoperatively was indicative of hyperfibrinolysis for which TXA was given. She was hypotensive throughout the case requiring a phenylephrine infusion and received 5.8 L of crystalloid and 1 liter albumin with estimated blood loss of 1.5 L. She was extubated on post-operative day (POD) 2 and discharged from the hospital on POD 12.

 Shortly following launching of this case, another emergency was listed involving a 49 year old female with a Type I thoracic aortic dissection. Ironically, this patient also carried the diagnosis of EDS Type IV and had previously undergone coronary artery bypass graft (CABG) for spontaneous right coronary artery dissection. Airway examination was significant for history of mandibular jaw surgery, limited mouth opening and mandibular gingival recession with multiple loose teeth. A radial arterial line was placed followed by an uneventful induction and intubation with video laryngoscopy. Central access via the right internal jugular vein was obtained with ultrasound guidance. She underwent uncomplicated ascending aorta replacement under deep hypothermic circulatory arrest.
She received 2.8 L crystalloid, 470 mL Cell saver, and 1 unit platelets with estimated blood loss of approximately 900 mL. She was extubated on POD 1 and discharged from the hospital on POD 7.

Discussion:

These cases detail the primary presentations (hallow organ rupture and vascular rupture/dissection) of Type IV Ehlers Danlos syndrome and the primary reason for increased mortality in this condition. The first patient had intraoperative coagulopathy that can be seen in EDS, especially types IV, VI, and VIII. Most patients do not have a specific hemostatic deficiency though bleeding times may be prolonged in those with reported bleeding history. Normalization of bleeding times have been shown in patients treated prophylactically with desmopressin prior to surgery. Hyperfibrinolysis is not a classical finding, however, and it was hypothesized that it may have been secondary to DIC in the setting of likely distributive shock due to perforated viscus. TEG was invaluable in guiding management in this case. The second patient had no abnormal bleeding throughout the Type I aortic dissection repair under circulatory arrest. She received only 1 unit of platelets in the postoperative period.

Both patients had limited mouth openings which can be seen with EDS given the association with temporomandibular dysfunction and jaw surgery. Furthermore the second patient had severe early onset gingival fragility and periodontitis, which is a noteworthy dental indicator of the disease. Clinically this holds great significance in cardiac surgery not only secondary to oral intubation but also placement and manipulation of the transesophageal echocardiography (TEE) probe.

Conclusion:

Type IV (vascular subtype) is the only subtype of Ehlers-Danlos syndrome with increased risk of mortality. Anesthetic considerations include the following:

- Avoid intramuscular injections and limit nasal or esophageal instrumentation due to bleeding risk.
- Minimize trauma during laryngoscopy to limit bleeding and utilize smaller endotracheal tube to minimize mucosal damage. Difficult airway management may be secondary to temporomandibular dysfunction, premature spondylosis, or occipitalatlantoaxial instability.
- Inquire pre-operatively about dental disease, especially in cardiac anesthesia given necessity for placement and manipulation of TEE probe.
- Monitor IV sites closely as extravasation of intravenous fluids may go unnoticed secondary to skin laxity. Also avoid excessive skin adhesives and tape secondary to skin friability. Careful padding during surgical positioning should occur to limit risk of injury to skin, joints, vessels and nerves.
- Maintain low airway pressures during positive pressure ventilation given risk of pneumothorax.
- Carefully consider need for arterial and central lines given hematoma and dissection risks. If lines are necessary, utilize ultrasound to limit risk of repeated vascular puncture.
- Bleeding time is the only abnormal hematologic assay. Consider the prophylactic use of desmopressin to assist with intraoperative coagulation in those with a bleeding history. If necessary utilize TEG to further guide management.
- Carefully weigh the risks and benefits of tourniquet use with the surgeon given risk of diffuse bleeding, compartment syndrome, and hemorrhagic shock.

- Avoid neuraxial techniques based on lack of clear benefit and potential risks of tissue friability and bleeding. Furthermore given bleeding risks, strongly consider avoiding peripheral nerve blocks.