of 31 patients, Dr Cameron mentions that he is reassessing the use of only 3 subannular sutures in patients who have extreme tissue fragility.⁴

Fukunaga and coauthors¹ provide a very important contribution and a modification of their technique; in recognition of the extreme fragility of the commissural triangles of the noncoronary cusp, they added 3 horizontal 4-0 polypropylene mattress sutures to this “paper-thin area.” They provide an illustrative drawing. The authors do not precisely state it, but they bestow a lesson for all of us. With the very wide and expanding clinical application of valve-sparing root replacement, there remain specific circumstances and genetic conditions with the severest of tissue fragility in which the technical expertise of the most experienced aortic

root surgeons, including the legendary Tirone David, may be necessary to achieve the desired long-term results.

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Commentary: Genetics and surgical planning in heritable aortic disease—moving from “when to operate” to “how to operate”

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The efficiency and decreasing cost of genetic analysis have increased the identification of gene mutations associated with heritable thoracic aortic aneurysm and dissection

Filamin A links aortic smooth muscle cell contractile units to the extracellular matrix.

CENTRAL MESSAGE

Consistent reporting of tissue quality and repair techniques used in patients with heritable aortic disease will help surgeons develop an operative plan tailored to a patient's genetic mutation.

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(HTAAD). Curating causative genes requires carefully evaluating the disease phenotypes associated with each mutation.¹ Consistently reporting gene-specific clinical features has been important in the development of evidence-based recommendations with which to counsel patients with HTAAD and make decisions about the timing of aortic repair.^{2,3} From a surgeon's perspective, knowing the tissue quality and recommended repair techniques

FIGURE 1. Filamin A links aortic smooth muscle cell contractile units to the extracellular matrix. SMC, Smooth muscle cell. Used with permission of Baylor College of Medicine.

associated with a mutation is also important when evaluating a patient with HTAAD preoperatively.

The article by Fukunaga and colleagues,⁴ from an extremely experienced center that has made seminal contributions to the field, details their experience with uncommonly fragile tissue and the technical adjustments made to complete a valve-sparing aortic root replacement in a patient with HTAAD. This patient was found preoperatively to have a causative mutation in *FLNA*, an X-chromosome gene that codes for filamin A, an actin binding protein involved in the aortic mechanotransduction complex (Figure 1). As one of the proteins linking actin contractile filaments within smooth muscle cells to the extracellular matrix, filamin A plays a key role in maintaining mechanical homeostasis of the aortic wall.^{5,6} Mutations in *FLNA* have been linked to HTAAD and described as having a similar systemic phenotype to vascular Ehlers-Danlos syndrome.⁷ The tissue fragility described by the authors correlates with the challenges described by surgeons and alternative techniques needed in repairing arteries in those with vascular Ehlers-Danlos syndrome.⁸ The authors support modifying operative techniques in patients with significantly friable tissue to avoid pseudoaneurysm formation due to tissue tearing as described by Liu and colleagues,⁹ who detailed complications after valve-sparing aortic root repairs in patients with severe Loeys-Dietz syndrome (LDS). These modifications may not be necessary in all patients with LDS because, in general, LDS has been described as not having a consistently fragile tissue phenotype.¹⁰ Variations in tissue fragility may be due to mutation-specific or patient-specific

factors, and reporting the patient's complete clinical features may help inform surgeons about what to expect when evaluating similar patients.

These reports highlight the importance of understanding the technical implications of varying tissue types in HTAAD during surgical repair. Many causative mutations of HTAAD are rare, and surgical repairs in affected patients are performed infrequently even at the most experienced centers. Although best practices are typically informed by large studies, such studies are probably not feasible in the less common types of HTAAD. The report by Fukunaga and colleagues⁴ and other reports of the gene-specific “intraoperative phenotype” of HTAAD provide valuable information for planning operative intervention. Although preoperative planning cannot replace intraoperative tissue evaluation, it can still be beneficial to anticipate the additional operative approaches that may be needed, particularly in patients with rare mutations. Anticipating which gene mutations—and potentially even which mutation variants—may necessitate modification of operative techniques provides an opportunity to expand precision medicine to the operating room in patients with HTAAD.

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