See Article page 16.

Commentary: How aggressive should we be in a prophylactic surgery for patients with Loeys–Dietz or Marfan syndrome?

Bo Yang, MD, PhD

As we understand more about the risks of aortic dissection and rupture in syndromic patients, such as those with Loeys–Dietz syndrome (LDS) and Marfan syndrome (MFS), and become better at valve-sparing aortic root replacement, more and more prophylactic aortic root replacements have been performed in those patients. It is always a question to surgeons as to how much distal aorta should be replaced (partial ascending aorta, entire ascending aorta, hemiarch, or total arch) as most patients with LDS or MFS have a normal-sized ascending aorta and aortic arch when they have the prophylactic aortic root replacement.

In this issue of the *Journal*, Seike and colleagues¹ studied the reoperation rate after initial operations in patients with LDS (n = 24) or MFS (n = 99) who had confirmed mutations in *TGFBR1*, *TGFBR2*, or *FBN1*. The authors excluded 45 patients who were diagnosed with MFS based on revised Ghent criteria but did not have genetic testing to confirm the diagnosis. This was appropriate, given the fact that patients with LDS can meet the clinical diagnostic criteria for MFS and only genetic testing can distinguish between LDS and MFS in these cases. In the LDS group, the authors only included patients with *TGFBR1* and *TGFBR2* mutations and excluded 2 patients with *SMAD3* mutations and 2 with *TGFB2* mutations. This was also appropriate since patients with *TGFBR1* and *TGFBR2* mutations have similar survival rate, aortic risk of dissection, and prevalence of extra-aortic features² but differ from patients with *SMAD3* mutations.³ Besides, no definitive conclusion or

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CENTRAL MESSAGE

As much of the ascending aorta as possible should be replaced during prophylactic aortic root replacement in LDS and MFS patients, with consideration for more aggressive arch replacement in LDS.

recommendation can be made based on just 2 patients with *SMAD3* and *TGFB2* mutations. After those patients were excluded, the sample size was smaller; however, the comparison was cleaner.

As expected, the authors found the LDS group had more total reoperations than the MFS group after initial operation. By focusing on each segment of the native aorta after initial surgery, they further determined only the reoperation of the aortic arch was significantly greater in LDS group compared with the MFS group. The indications for the arch reoperation were arch aneurysm and acute type A aortic dissection, which were appropriate inclusion criteria. However, both the LDS and MFS groups included patients with chronic dissected arch, 10% and 12%, respectively, which is more susceptible to reoperation than the non-dissected aortic arch. Only 11 patients in the LDS group and 58 patients in the MFS group had isolated root replacement as the initial operation. Nine patients with LDS had descending thoracic or thoracoabdominal aortic aneurysm replacement as their initial operations. It would be a cleaner study to include only the patients with virgin (non-dissected) arch after initial prophylactic root replacement to compare the reoperation rate between the LDS and

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MFS groups. Another interesting and clinically relevant observation was that 5 patients in the MFS group and 4 patients in the LDS group still developed type A aortic dissection after aortic root replacement.

Based on the findings in this study, along with similar findings from Hopkins group⁴ and a report of 441 patients with *TGFBR1* and *TGFBR2* mutations from the Montalcino Aortic Consortium,² we would agree that as much of the ascending aorta as possible should be resected during prophylactic aortic root replacement in patients with LDS or MFS. More arch replacement could be performed in patients with LDS, but it is still not clear whether either a hemiarch or total arch replacement should be routinely performed. Just like MFS, not every patient with LDS behaves the same due to different gene mutations (*TGFBR1* vs *TGFBR2*) and mutations at different sites in the same gene. More aggressive prophylactic aortic root and arch replacements should be considered in patients with LDS with arterial/aortic tortuosity and severe extra-aortic features,

which may serve as biomarkers of more severe and aggressive vascular disease.² A less-aggressive surgical management strategy could be pursued in the absence of any familial event or rapid increase in aortic diameter, especially in women harboring *TGFBR1* mutations who on average have later onset aortic disease than men with *TGFBR1* mutations.²

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See Article page 16.

Commentary: Prophylactic total arch replacement in Loeys–Dietz syndrome: Perfect may be the enemy of good

Ivancarmine Gambardella, MD, and
Leonard N. Girardi, MD

In this issue of *The Journal*, Seike and colleagues¹ compared the surgical fate of 123 patients with 2 genetically distinct heritable aortopathies (HAPs): Marfan syndrome (MFS) and Loeys–Dietz syndrome (LDS). The authors

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CENTRAL MESSAGE

In experienced hands, prophylactic total arch replacement may reduce the need for reoperation in patients with Loeys–Dietz syndrome.

should be commended for their outstanding surgical skills, which resulted in no operative mortality or permanent neurologic deficit in this complex cohort. The reoperation rate for native aortic segments at 10-year follow-up was

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