Commentary

Marfan syndrome is the main independent predictor of recurrent aortic dissection in patients enrolled in the International Registry of Aortic Dissection (IRAD)

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In the October 2016 issue of *Circulation* (1), Isselbacher and colleagues published their observations regarding patients with recurrent aortic dissection enrolled in the International Registry of Aortic Dissection (IRAD).

Isselbacher and colleagues included 3,828 patients that suffered from acute aortic dissection (AAD) and among these, 204 were identified that presented with recurrent aortic dissection (RAD) during follow-up.

The authors showed that while RAD is quite rare it does happen and interestingly follows certain patterns in terms of patient demographics and anatomical variables. Patients presenting with RAD were slightly younger on average (in this group of patients, the percentage of elderly patients—>70 years—was very low). More than half of the RAD patients suffered from type B dissection at some point compared to only one-third in those without RAD. Initial presentation with type B dissection was also more frequent in patients with RAD (28%) compared to those who did not have a second event (11%). Diameter of the descending aorta was significantly larger in patients with RAD compared to non-RAD patients whether they presented with Stanford type A or type B dissection.

Most probably, the majority of differences between patients suffering from RAD and those that did not have a second event can be explained by the much higher prevalence of patients with Marfan syndrome (MFS) in the RAD group. In the group of patients with RAD, 22% of patients were diagnosed with MFS compared to 3% in those without RAD.

In the current study, MFS was the strongest independent risk factor for RAD with a HR of 8.6. Other important risk factors for RAD in the non-MFS patient population were known aortic aneurysms (HR 8.3), history of aortic valve replacement (HR 3.6) and non-white race (HR 2.1). Interestingly, bicuspid aortic valve (BAV) did not appear to be a risk factor for RAD, maybe indicating that BAV is a risk factor for development of aortic aneurysms but not necessarily associated with a higher susceptibility for acute dissection.

As detailed anatomical and imaging data were not available for the vast majority of patients enrolled in IRAD, Isselbacher and colleagues identified a subset of 50 patients followed in 2 (!) of the centers, added 13 non-IRAD patients and performed an in-depth chart and imaging review. In this group of 63 patients, more patients suffered from type B dissection and later presented with type A dissection (54%) than vice-versa (42%).

From a "definition" point of view, it seems very difficult to ensure that all RAD patients in IRAD had a true de-novo type B dissection after type A dissection as this might have required detailed imaging analysis over time. This assumption would require the proof that the initial dissection was completely excluded following initial surgery. Furthermore, the authors did not elaborate whether the initial surgical strategy, e.g., partial or complete aortic

arch replacement and the use of a frozen elephant trunk influenced the risk of further events. In the current report, there was almost a decade between the initial events and RAD. While there was no increased rate of major early complications, more patients with RAD underwent open repair and/or TEVAR after the event. Again, it has already been shown that type B dissection in MFS patients is a strong risk factor for aortic re-interventions and associated with a high need for replacement of the entire thoracoabdominal aorta.

As more and more patients undergo elective aortic root repair to prevent Stanford type A dissection, morbidity and mortality in patients with MFS has shifted away from the aortic root towards the more distal aorta. Analysis of the Euro Heart Survey database revealed that 31% of interventions in patients with MFS have been performed on the distal aorta (2). Other reports show that already 18% of primary interventions are due to lesions on the distal aorta (3). We and others have shown that AAD is the main risk factor driving the need for re-interventions in MFS (4).

Prediction of type B dissection in MFS patients is difficult since the vast majority of patients dissect while the diameter of the descending aorta is still well below the accepted threshold for prophylactic surgery. The current data shows that the diameter of the descending aorta at the time of dissection is larger in patients with RAD than in those without. But even in those RAD patients presenting with type B dissection, the mean diameter is below the threshold for prophylactic surgery recommended in the most recent guidelines. Do we further believe that the aorta expands immediately during dissection (5) it becomes clear that foreseeing recurrent events in the descending aorta will remain a challenge.

The presence of MFS in patients with acute dissection has a dramatic effect on the rate and nature of recurrent dissection. As the authors already discussed, over the past decade, the medical community has slowly accepted the idea that patients presenting with aortic aneurysms and dissections are part of a wide spectrum of genetically mediated diseases that present in syndromic as well a non-syndromic forms.

MFS has long been the only seriously considered differential diagnosis in terms of a heritable disorder of connective tissue in patients with aortic aneurysm. We recently performed retrospective testing for mutations in the genes encoding for the TGFb receptors 1 and 2 in patients that underwent aortic surgery under the assumption of having MFS but tested negative for FBN1 mutation before the Loeys-Dietz syndrome (LDS) was recognized and defined as separate connective tissue disease and identified 20% of patients as having LDS (6).

Therefore we strongly believe that a closer look at the IRAD patients including formal evaluation and subsequent genetic testing would identify new subsets and patterns of dissection and recurrent dissection in this patient population.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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