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ORIGINAL ARTICLE

Aortic Root Dilation: Do Patients With Marfan Syndrome Fare Worse Than Those With Marfanoid Features?

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Abstract

Objective: To discover whether patients with aortic root dilation and leptosomic features but without a diagnosis of Marfan syndrome (MFS) fare similarly to patients with MFS.

Methods: Of 124 patients with aortic root dilation identified from August 1, 1994, through October 31, 2012, 66 had MFS and 58 had leptosomic features but did not meet the Ghent criteria. Genetic testing was performed in 35% of patients (n=43). We compared *z* scores and aortic root diameters for patients who presented with aortic root dilation with and without an MFS diagnosis and with and without aortic root repair.

Results: No difference existed in initial aortic root diameters between groups (P=.15); however, mean ± SD *z* scores for patients without MFS and with MFS were 3.1±2.3 vs 4.5±3.2 (P=.005). Fourteen of 58 patients (24%) without MFS and 35 (53%) with MFS underwent aortic root operations (P<.05). For both groups who did not have surgery, aortic root diameters and *z* scores remained similar at follow-up (P=.20), as did 10-year survival: MFS, 100%; no MFS, 94.1% (P=.98). No significant difference was found for mean ± SD root diameter (no MFS, 38.9±7.3 mm; MFS, 35±8.6 mm; P=.06) or *z* score (no MFS, 2.4±2.0; MFS, 2.1±2.0; P=.53) for patients who underwent surgery. Two patients in each group had aortic root dissections.

Conclusion: Similar rates of aortic dissection between the 2 groups warrant further study regarding patients with leptosomic features but no diagnosis of MFS. Aortic root dilation progressed similarly in patients who did not undergo surgery.

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Before 1996, the Berlin criteria were used to establish the diagnosis of Marfan syndrome (MFS) in patients who had nonspecific clinical findings of connective tissue disease. In 1996, the more stringent Ghent nosology became the standard for diagnosing MFS. With their 2010 revision, the Ghent criteria were again refined to allow for better specificity, but this came with uncertain true sensitivity.[1] The strict Ghent criteria may leave patients with leptosomic features and aortic root dilation without a unifying diagnosis, ultimately leading to a prognostic dilemma regarding the dilated aortic root. Should these patients be treated similar to those in the general population or managed similar to patients with MFS regarding aortic operation? To help clarify this issue, we undertook a retrospective study using *z* scores and aortic root diameters to compare outcomes of patients who have aortic root dilation and leptosomic features, with and without an MFS diagnosis.

METHODS

This study was approved by the Mayo Clinic Institutional Review Board. We reviewed electronic health records from August 1, 1994, through October 31, 2012, of 489 consecutive patients who were initially evaluated in our Thoracic Aortic Clinic and then were referred to our geneticists for possible concern of a genetic disorder. Patients diagnosed as having genetic disorders other than MFS were excluded. Patient records were cross-referenced with our echocardiography

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and radiology (computed tomography and magnetic resonance imaging) databases by using the keywords *annuloaortic ectasia*, *aortic root aneurysm*, *aortic root dilation*, *aortic root dilatation*, and *aortic root size greater than 30 mm*. From this review, 124 patients with aortic root dilation were identified; these patients composed the study group. *Z* scores and diameters were noted at the initial visit to the clinic and at the operation or at the latest follow-up from the reports of imaging (computed tomography or echocardiography) at that time. Time to aortic dissection, rupture, or all-cause death was noted. Because cause of death was indeterminate for most patients, it was not used in the analysis. We calculated *z* scores for all patients with aortic root dilation by using the following equation: z = (measured diameter − predicted diameter)/0.261 cm. Predicted diameter (cm) = 2.423 + (age × 0.009) + (body surface area [BSA] × 0.461) − (sex × 0.267), where male sex = 1, female sex = 2.[2] All 124 patients had a genetic consultation, and 35% (n=43) underwent genetic testing. Diagnosis of MFS was made clinically according to the Ghent criteria (determined by time of initial clinic visit over the 18-year time frame) or with genetic testing. Leptosomic features refer to characteristics of patients who are tall and slender, with long hands and associated musculoskeletal or ocular abnormalities. Follow-up was calculated from the initial visit to the operation or to the most recent visit that included imaging of the aorta.

Statistical Analyses

Descriptive statistics for categorical variables are reported as frequency and percentage, and continuous variables are reported as mean ± SD. Categorical variables were compared between 2 groups by using the χ^2 test or Fisher exact test, and continuous variables were compared using a 2-sample *t* test or Wilcoxon rank sum test, as appropriate. The Kaplan-Meier method was used to compile data for survival curves and calculate 5- and 10-year survival statistics. All the statistical tests were 2-sided, with the alpha level set at .05 for statistical significance. All the statistical analyses were performed using statistical analysis software (SAS; SAS Institute Inc).

RESULTS

Of the 124 patients who had aortic root dilation, 66 had MFS and 58 had leptosomic features and did not meet the Ghent diagnostic criteria for MFS. Of the 58 patients without MFS, 74% were men (n=43; *P*=.15), with a mean ± SD age of 36±19 years and a mean ± SD BSA of 1.9±0.4 m^2. Of 66 patients with MFS, 70% were men (n=46), with a mean ± SD age of 28±17 years (*P*=.004) and a mean ± SD BSA of 1.9±0.6 m^2. The mean ± SD root diameter was 41.1±8.0 mm for patients without MFS and 43.3±10.7 mm for patients with MFS (*P*=.15). A significant difference existed in mean ± SD *z* scores for patients without MFS (3.1±2.3) compared with those of patients with MFS (4.5±3.2) (*P*=.005). Median follow-up was 2.3 years (range, 0-13.9 years). We had 96% follow-up for imaging.

Genetic testing was performed in 18 patients (31%) without MFS. Of these patients, only 2 (11%) had a mutation detected. One mutation was an *FBN2* gene variant, p.I2394T, which is a variant of unknown significance. The other patient had 2 variants of the *MYH11* gene of unknown significance (p.K1256Q and p.T253M). Genetic testing was performed in 25 patients (38%) with MFS. Seven of these patients (28%) did not have an identifiable mutation, and the diagnosis of MFS was made on clinical criteria.

Patients Undergoing Surgery

Only 14 patients (24%) without MFS and 35 patients (53%) with MFS underwent aortic root repair, with mean ± SD *z* scores of 5.0±2.0 (without MFS) and 6.4±2.6 (MFS) (*P*=.05). At the time of operation, the mean ± SD aortic root diameter was 48.3±5.1 mm for patients without MFS and 50.5±6.5 mm for patients with MFS (*P*=.66). Of the 14 patients without MFS who underwent surgery, 11 had aortic root replacements within 3 months of their first visit. The 3 other patients were followed up for a mean ± SD of 74.5±17.9 months before operation. Seven patients had a composite valved conduit root replacement, and 6 had a valve-sparing aortic root replacement. The remaining 1 patient had an aortic valve repair with a primary aortoplasty. Of the 35 patients with MFS who underwent operation, 30 had aortic root replacements within 3 months of their first visit.

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