ORIGINAL RESEARCH

Aortic Complications Associated With Pregnancy in Marfan Syndrome: The NHLBI National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC)

Mary J. Roman, MD; Norma L. Pugh, MS; Tabitha P. Hendershot, BA; Richard B. Devereux, MD; Hal Dietz, MD; Kathryn Holmes, MD, MPH; Kim A. Eagle, MD; Scott A. LeMaire, MD; Dianna M. Milewicz, MD, PhD; Shaine A. Morris, MD, MPH; Reed E. Pyeritz, MD, PhD; William J. Ravekes, MD; Ralph V. Shohet, MD; Michael Silberbach, MD; for the GenTAC Investigators*

***Background*—**The risk of aortic complications associated with pregnancy in women with Marfan syndrome (MFS) is not fully understood.

***Methods and Results*—**MFS women participating in the large National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC) were evaluated. Among 184 women with MFS in whom pregnancy information was available, 94 (51%) had a total of 227 pregnancies. Among the women with pregnancies, 10 (10.6%) experienced a pregnancy-related aortic complication (4 type A and 3 type B dissections, 1 coronary artery dissection, and 2 with significant [≥3 mm] aortic growth). Five of 7 aortic dissections, including all 3 type B, and the coronary dissection (75% of all dissections) occurred in the postpartum period. Only 5 of 8 women with pregnancy-associated dissection were aware of their MFS diagnosis. The rate of aortic dissection was higher during the pregnancy and postpartum period (5.4 per 100 person-years vs 0.6 per 100 person-years of nonpregnancy; rate ratio, 8.4 [95% CI=3.9, 18.4]; $P<0.0001$).

***Conclusions*—**Pregnancy in MFS is associated with an increased risk of aortic dissection, both types A and B, particularly in the immediate postpartum period. Lack of knowledge of underlying MFS diagnosis before aortic dissection is a major contributing factor. These findings underscore the need for early diagnosis, prepregnancy risk counseling, and multidisciplinary peripartum management. **(*J Am Heart Assoc*. 2016;5:e004052 doi: 10.1161/JAHA.116.004052)**

Key Words: aneurysm • aortic disease • aortic dissection • Marfan syndrome • pregnancy and postpartum

Estimates of the risk of cardiovascular complications, primarily aortic dissection, associated with pregnancy in women with Marfan syndrome (MFS) have varied widely. Complication rates may be systematically overstated because of publication bias, ascertainment bias, case reports or small sample size, and inclusion of women whose aortic dissection precedes and results in the diagnosis of MFS. Women who are aware of their underlying diagnosis may receive prepregnancy counseling, choose to forego pregnancy, have careful monitoring and take beta-blockers during pregnancy, or undergo prophylactic aortic surgery in anticipation of pregnancy, if indicated.

In addition, few serial imaging data to permit correlation of aortic diameters with risk of progressive dilatation and/or

From the Division of Cardiology, Weill Cornell Medical College, New York, NY (M.J.R., R.B.D.); Biostatistics and Epidemiology Division, RTI International, Rockville, MD (N.L.P., T.P.H.); Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD (H.D., W.J.R.); Department of Pediatrics, Oregon Health & Sciences University, Portland, OR (K.H., M.S.); Division of Cardiology, University of Michigan Health System, Ann Arbor, MI (K.A.E.); Divisions of Cardiothoracic Surgery (S.A.L.) and Pediatric Cardiology, Department of Pediatrics (S.A.M.), Baylor College of Medicine, Houston, TX; Department of Internal Medicine, McGovern Medical School, University of Texas Health Science Center, Houston, TX (D.M.M.); Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA (R.E.P.); Department of Medicine, John A. Burns School of Medicine, Honolulu, HI (R.V.S.).

*A complete list of the GenTAC Investigators can be found in the Appendix at the end of the article.

Correspondence to: Mary J. Roman, MD, Division of Cardiology, Weill Cornell Medical College, 520 E 70th St, New York, NY 10021. E-mail: mroman@med.cornell.edu

Received June 10, 2016; accepted July 14, 2016.

dissection associated with pregnancy are available. As a consequence, recommendations regarding aortic root dimensions above which pregnancy is discouraged vary[1–5] and are based on limited historical imaging data.[1,2] Furthermore, reported event rates may be confounded by prepregnancy counseling.

The National Heart, Lung and Blood Institute–sponsored National Registry of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC) offers an opportunity to address some of these limitations by providing comprehensive information on a large population of well-characterized patients with MFS.

Methods

Study Population

The rationale and design of the GenTAC have been previously described.[6] In brief, GenTAC was established as a longitudinal observational cohort study of individuals with genetically triggered thoracic aortic aneurysm. Between 2006 and 2014, 3700 participants were enrolled in the original 6 centers (Johns Hopkins University, Baylor College of Medicine, Oregon Health & Sciences University, University of Pennsylvania, University of Texas Health Science Center at Houston, and Weill Cornell Medical College) and the 2 additional centers (National Institute of Aging–Harbor Hospital and Queen's Medical Center) added in the second phase.[7] Standardized data collection included clinical information, patient questionnaire, imaging studies, and details of surgical interventions. A core phenotyping laboratory provided validation of eligibility diagnoses. Institutional review board approval was obtained for this study at each of the 8 participating GenTAC regional clinical centers. Individual informed consent was obtained from each GenTAC Registry patient.

At the conclusion of registry enrollment (December 31, 2013), 893 patients with Marfan syndrome had been enrolled in the GenTAC database, of whom 298 were women over the age of 17 years. Of these, 184 (62%), who completed and returned the Enrollment Patient Questionnaire and included information on presence or absence of pregnancy, form the basis for the current analyses. Requested information for each pregnancy included age at pregnancy, outcome of pregnancy, and complications during and after pregnancy, including aortic dissection and aortic growth.

Based on questionnaire responses, as well as data on pre-enrollment occurrence of aortic dissection or prophylactic aortic surgery provided by the clinical centers, more-detailed information was requested regarding all women with aortic complications. Aortic complications were defined as aortic dissection, excessive aortic growth (≥3 mm) during pregnancy, and need for prophylactic proximal aortic surgery because of large or rapidly expanding aneurysm. Because virtually all pregnancies preceded enrollment in the GenTAC registry, imaging data regarding peripartum aortic diameters were not systematically available. In those women who indicated significant aortic growth had occurred during pregnancy in the patient questionnaire, supporting data were retrospectively requested from the clinical center. Data regarding medication use during pregnancy, method of delivery, and breastfeeding were not available.

Statistical Analysis

Demographic and phenotypic characteristics of never-pregnant and ever-pregnant women with MFS were compared using an independent-samples *t* test for continuous variables and Fisher's exact test for categorical variables. In order to determine age-adjusted rates of aortic surgery and dissection, the period of exposure to need for prophylactic aortic surgery and acute aortic dissection was calculated by subtracting 15 (presumed age at which pregnancy and associated dissection risk might begin) from the age of enrollment in GenTAC (to determine the number of years of risk before enrollment) and multiplying by the number of women in the given group. Pregnancy exposure was considered to occupy 1 year, including the 3-month postpartum period. Ninety-five percent confidence intervals were generated using the log of the rate ratio and the standard error of its log and then calculating the exponential. Rate ratios were compared using a generalized linear model with a Poisson probability distribution and a log link function.

Results

Pregnancies

Among 184 women in whom pregnancy information was available, 94 (51%) reported a total of 227 pregnancies (mean, 2.5; median, 2.0; range, 1–6). Average maternal age was 29 and ranged from 13 to 43 years (2 women who had pregnancies before the age of 18 are included in the analysis). Pregnancy outcomes included 147 live births (2 sets of twins), 3 still births, 30 miscarriages, 38 abortions, 3 ectopic pregnancies, and 3 ongoing pregnancies; 3 did not respond to the outcome question on the survey. Pregnancy was complicated by hypertension in 19, diabetes mellitus in 1, and premature rupture of membranes in 6. Women who completed the patient questionnaire were older at the time of enrolment (42 vs 36 years; P=0.002) and more likely to have had type B aortic dissection and prophylactic surgery than those who did not complete the questionnaire; however, the latter differences were eliminated when adjusted for differences in age.

Comparison of Never-Pregnant and Ever-Pregnant Women

Demographic and phenotypic features of ever-pregnant and never-pregnant MFS women are compared in Table 1. Women who never became pregnant were significantly younger at age of MFS diagnosis and at enrollment into GenTAC. Although heights were similar, never-pregnant women weighed significantly less. Average systemic score was higher in never-pregnant women. Phenotypic features that differed between the 2 groups included a significantly higher proportion with arachnodactyly, both wrist and thumb signs, and pes planus in never-pregnant women. In addition, never-pregnant women tended to have a higher proportion with thoracic skeletal abnormalities, such as pectus carinatum and kyphosis.

Table 1. Comparison of Demographic and Phenotypic Features in Never-Pregnant Versus Ever-Pregnant Women

	Never-Pregnant (n=90)	Ever-Pregnant (n=94)	*P* Value
Age at diagnosis, y	13±11	27±17	<0.0001
Age at enrollment, y	37±13	47±13	<0.0001
Height at enrollment, cm	176±9	177±8	0.45
Weight at enrollment, kg	70.7±14	76.8±15	0.007
SBP at enrollment, mm Hg	118±13	117±15	0.72
DBP at enrollment, mm Hg	69±10	69±14	0.95
Arm span, cm	176±24	175±28	0.97
Lower segment, cm	91±16	91±14	0.81
Pectus carinatum, %	34	24	0.08
Pectus excavatum, %	26	24	0.62
Scoliosis, %	62	59	0.44
Kyphosis, %	24	15	0.10
Pes planus, %	53	38	0.04
Lumbosacral dural ectasia, %	22	21	0.88
Spontaneous pneumothorax, %	11	12	0.90
Striae atrophicae, %	57	48	0.23
Wrist sign, %	61	44	0.0047
Thumb sign, %	65	46	0.0015
Ectopia lentis, %	47	43	0.46
Myopia >4 diopters, %	31	22	0.18
Mitral prolapse, %*	65	63	0.52
Systemic score	6.5±2.8	5.2±3.2	0.0025

DBP indicates diastolic blood pressure; SBP, systolic blood pressure.
*Ascertained from standardized clinical evaluation form.

At the time of GenTAC enrollment, ever-pregnant women were more likely to have had a previous aortic dissection (25 of 94 [27%] vs 13 of 90 [14%]; *P*=0.047) and more likely to have undergone prophylactic proximal aortic surgery (13 of 94 [14%] vs 4 of 90 [4%]; *P*=0.04). Prophylactic proximal surgery in ever-pregnant woman followed, rather than preceded, pregnancy in all instances. Ever-pregnant women who had an aortic dissection were less likely than never-pregnant women to be aware of their Marfan diagnosis before their dissection (8 of 25 [32%] vs 10 of 13 [77%]; *P*=0.016). Among the women who had not undergone proximal aortic surgery at time of registry entry and in whom imaging data were available (n=53), there were no differences in aortic root dimensions (3.9±0.47 vs 4.0±0.56 cm; *P*=0.44) or aortic root *Z* scores (3.4±1.75 vs 3.4±2.27; *P*=0.92) in never-pregnant versus ever-pregnant women, respectively, including following adjustment for differences in age between the 2 groups.

Aortic Complications Associated With Pregnancy

Among the 94 women with at least 1 pregnancy, 10 (10.6%) developed an aortic complication in the peripartum period (defined as pregnancy and 3 months postpartum), including 4 type A dissections, 3 type B dissections, 2 with significant (≥3 mm) aortic growth, and 1 coronary artery dissection. Details of these complications are presented in Table 2. Of note, all 3 type B dissections, 2 of the type A dissections, and the coronary artery dissection (overall, 75% of dissections) occurred in the postpartum period.

Knowledge of MFS Diagnosis Before Pregnancy and Before Aortic Dissection

Among the 94 ever-pregnant women, only 42% were aware of their diagnosis before their first pregnancy. Five of the 8 women who experienced pregnancy-related aortic or coronary dissections were aware of their diagnosis before the event. Aortic dissections not related to pregnancy occurred in 17 of the 84 ever-pregnant women, 8 of whom were aware of their diagnosis before the occurrence of the aortic dissection. Among the 90 never-pregnant women in whom 13 aortic dissections occurred, 10 were aware of their diagnosis before the dissection occurred. Thus, 12 of 30 (40%) non-pregnancy-related dissections occurred in women who were unaware of their diagnosis, whereas 60% occurred after the diagnosis.

Comparison of Ever-Pregnant Women With and Without Aortic Complications

Demographic and phenotypic features of pregnant women who did not have aortic complications are compared to those who did have complications in Table 3. There were no

Table 2. Aortic Complications Associated With Pregnancy

Patient	Pregnancy Age, y	Complication	Timing of Complication	Medication Use	Knowledge of Diagnosis	Outcome
1	36	Type A dissection	Peripartum	Beta-blocker	Yes	Dissection discovered after delivery with subsequent surgery
2	35	Type A dissection	Third trimester	No	No	Emergency Caesarian section followed by aortic surgery
3	34	Type A dissection	6 days postpartum	No	No	Emergency aortic surgery
4	25	Type A dissection	3 days postpartum	Other BP-lowering drug	Yes	Emergency aortic surgery
5	36	Type B dissection	6 weeks postpartum	Beta-blocker	Yes	Elective surgery for expanding aneurysm
6	29	Type B dissection	3 days postpartum	Unknown	Yes	Emergency aortic surgery
7	27	Type B dissection	1 day postpartum	No	No	Elective surgery 5 years later
8	33	Left main coronary artery dissection	2 weeks postpartum	No	Yes	Emergency coronary bypass surgery
9	28	Aortic growth (3.6–4.0 cm)	Pregnancy	None	Yes	Subsequent surgery for type A dissection
10	34	Aortic growth (4.7–5.3 cm)	Pregnancy	Beta-blocker	Yes	Caesarian section; aortic surgery 6 months postpartum

BP indicates blood pressure.

significant differences between the 2 groups. In addition, the mean number of pregnancies did not differ between those without and with aortic complications (2.5 vs 2.4; P=0.82). Use of beta-blocking agents was more common at the time of enrollment in those with complications (50% vs 13%; P=0.012).

Impact of Pregnancy on Rates of Aortic Dissection and Prophylactic Surgery

The rate of prophylactic proximal aortic surgery among ever-pregnant women was 0.43 per 100 patient years (95% CI=0.198, 0.668) and 0.20 per 100 patient-years (95% CI=0.004, 0.405) among never-pregnant women (rate ratio=2.12 [95% CI=0.690–6.494]; P=NS). Aortic dissection rates associated with pregnancy and the postpartum period were significantly higher than nonpregnancy dissection rates (5.4 per 100 person-years [95% CI, 1.7, 9.2] vs 0.6 per 100 patient-years [95% CI=0.42–0.87]; rate ratio=8.4 [95% CI=3.9–18.4]; P<0.0001).

Discussion

The GenTAC Registry represents the largest analysis to date of pregnancy risk in women with MFS. Our results underscore the risk of the peripartum period for aortic dissection. The rates of aortic dissections unrelated and related to pregnancy (0.6 and 5.4 per 100 patient-years) noted in the GenTAC Registry far exceed recently published population-based rates of aortic dissection among women (0.0024 per 100 patient-years in Oxfordshire, UK,[8] and 0.0029 per 100 patient-years in Emilia-Romagna, Italy[9]). The lack of knowledge of underlying MFS diagnosis in almost 50% of registry women with aortic dissection related to pregnancy is a common finding in the existing literature and underscores the need for early diagnosis, prepregnancy risk counseling, and multidisciplinary peripartum management.[5,10]

The early literature on pregnancy risk in women with MFS is limited to publication of single case reports[11–14] or very small series.[15–17] In addition, the diagnosis of MFS was not always firmly established, but presumptive, based on non-specific skeletal features[12,16,17] or in the setting of underlying bicuspid aortic valve,[15] a known risk factor for aortic aneurysm and dissection. Furthermore, some women with a firm diagnosis of MFS at the time might have actually had Loeys-Dietz syndrome, which had not yet been described and may carry a higher risk of dissection than MFS. In contrast, MFS diagnosis in the present study was based on systematic application of revised Ghent criteria[18] with central review by the GenTAC Phenotyping Core.

The first large series, published in 1981 with the goal of providing a more-representative assessment of pregnancy

Table 3. Comparison of Demographic and Phenotypic Features in Pregnant Women Without Versus With Aortic Complications*

	No Aortic Complication (n=84)	Aortic Complications* (n=10)	*P* Value
Age at diagnosis, y	27±16	22±11	0.31
Age at enrollment, y	47±14	42±13	0.26
Age at first pregnancy, y	26±6	25±8	0.55
Number of pregnancies	2.5±1.4	2.4±1.1	0.89
Height at enrollment, cm	177±8	177±9	0.91
Weight at enrollment, kg	77.0±15	74.2±14	0.60
SBP at enrollment, mm Hg	117±14	118±13	0.73
DBP at enrollment, mm Hg	70±13	66±10	0.06
Arm span, cm	175±25	179±24	0.76
Lower segment, cm	91±15	92±16	0.98
Pectus carinatum, %	34	24	1.0
Pectus excavatum, %	23	50	0.12
Scoliosis, %	62	70	0.74
Wrist sign, %	48	40	0.75
Thumb sign, %	49	50	1.0
Ectopia lentis, %	46	40	0.75
Mitral prolapse, %†	75	70	0.29

DBP indicates diastolic blood pressure; SBP, systolic blood pressure.
*Coronary artery dissection patient is included in this group.
†Ascertained from standardized clinical evaluation form.

risk, included 105 pregnancies in 26 women with MFS seen at the Johns Hopkins Medical Genetics Clinic.[1] Twelve of these 26 women had evidence of cardiovascular disease (heart murmurs in 6, mitral prolapse in 2, "some degree of aortic dilatation" in 3, and palpitations in 1). Three of the 12 women had cardiovascular complications (transient murmur, progressive heart failure attributed to severe mitral regurgitation, or atrial tachycardia); there were no aortic complications. The number of women having echocardiograms was not provided, but none were reported to have aortic root diameters over 42 mm. Based on these data, Pyeritz recommended against pregnancy in women with aortic diameters over 40 mm.[1]

A subsequent prospective study of 45 pregnancies in 21 women with MFS evaluated at Johns Hopkins between 1983 and 1992 noted aortic dissections in 3 women,[19] 1 type B dissection at 20 weeks' gestation (previously published as a case report by Mor-Yosef et al[16]), a type A dissection misconstrued as rapid aortic expansion until elective surgery postpartum, and distal extension of a previous type A dissection operated upon before pregnancy and occurring postpartum in the setting of intravenous drug use. Importantly, echocardiographic surveillance was performed in 22 of 28 pregnancies carried through the third trimester with "little or no change in aortic root diameter during pregnancy."

More-recent studies have provided somewhat more-comprehensive peripartum imaging data to permit better assessment of risk of aortic complications. In a Dutch study of 127 women with MFS evaluated between 1993 and 2004, 61 had been pregnant, of whom 23 women with 33 pregnancies had aortic dimensions determined by echocardiography (only 10 before and after pregnancy).[4] Only 1 woman, with a previous type A dissection, developed a type B dissection during her second pregnancy. Nine of the other 22 women had aortic root diameters ≥40 mm (range, 40–45) with insignificant pregnancy-associated diameter change. Based on these data, the investigators suggested that pregnancy in the absence of pre-existing aortic dissection is safe up to 45 mm.

The most comprehensive study to date including imaging data involved 69 women with a total of 199 pregnancies evaluated in Salt Lake City[5]; 32 of these women were aware of their MFS diagnosis, had not had previous aortic surgery, and were followed prospectively for a total of 52 pregnancies. In 14 pregnancies (27%), aortic root diameter was ≥40 mm. Although there were no aortic peripartum complications, women who had been pregnant were more likely to receive prophylactic aortic surgery than the 29 never-pregnant women (13.0% vs 6.5%; *P*=0.03), similar to findings in the current study. However, because women in our study who had had pregnancies were older than those who had never been pregnant, there was no significant difference between the 2 groups in annual rate of proximal aortic surgery. None of the 69 women with pregnancies in the Salt Lake City study experienced a peripartum dissection, and none of the nulliparous women experienced aortic dissection. Lower rates of aortic dissection in these women, compared to GenTAC women, may be attributed to older age in the latter cohort and hence longer duration of exposure.

Lack of knowledge of the underlying diagnosis of MFS was common in pregnancy-associated aortic dissection in the GenTAC Registry as well as in earlier reports. In an English registry including 36 women with MFS, 6 women had pregnancy-related complications.[20] Three of 4 women with acute dissections and both women with rapid aortic expansion necessitating postpartum surgery were unaware of their MFS diagnosis before their pregnancies. In a letter survey sent to members of the Dutch Marfan Association, 5 aortic dissections occurred in 44 women, only 3 of whom were aware of their diagnosis.[21] In a retrospective analysis of a

French outpatient MFS clinic, 7 of 85 women suffered a peripartum aortic complication, only 3 of whom were aware of their diagnosis.[22] The same group followed 18 women prospectively using standardized guidelines, including serial echocardiography, beta-blockade therapy, and tailored delivery approaches.[10] The sole aortic dissection occurred in a woman referred at 35 weeks of pregnancy with an aortic diameter of 47 mm who had an acute type A dissection at 37 weeks just before a planned cesarean delivery. In the current study, the significantly earlier age at diagnosis of MFS in the never-pregnant group (13±11 vs 27±17 years) may have influenced recommendations and decisions regarding reproduction.

MFS is classically associated with proximal aortic dilatation; accordingly, type A dissections are much more common than dissections exclusively involving the distal aorta. Among 100 MFS patients with aortic dissection, 80% involved the ascending aorta whereas 20% were isolated to the descending aorta.[23] Strikingly similar results were reported in a Swiss population, wherein initial aortic dissection was type A in 77% and type B in 23%.[24] Thus, it is noteworthy that 3 of the 7 aortic dissections in our series were type B dissections, all of which occurred in the postpartum period and none of which were associated with previous proximal aortic surgery. Although cardiac output is increased during pregnancy because of increases in stroke volume and heart rate, substantial further increases occur in association with labor and delivery, potentially further increasing pulsatile stress on the aorta. Type B dissections have been described in previous reports[4,13–16,21,22]; of these, 5 of 8 were postpartum. Reports of postpartum type A dissection are less common,[21,25] including 1 of 3 in our series.

Study Limitations

There are several potential limitations to the current study. Although aortic dissection is unlikely to go unrecognized and miscategorized, the prevalence of significant aortic growth may be underestimated because of reliance on the patient questionnaire. However, all such instances reported on the patient questionnaire were further explored through clarification by site investigators. In addition, we did not collect systematic peripartum imaging data because the pregnancies predated participation in the registry (average age of pregnancy 29 years vs average age at enrollment of 47 years). The lack of systematic peripartum imaging data in the GenTAC cohort precludes assessment of pregnancy risk based on aortic dimensions. Another limitation includes the lack of systematic information about peripartum medication use and lactation given the retrospective ascertainment of pregnancy data. Although the sites involved in GenTAC were, of necessity, referral centers for patients with genetically mediated thoracic aortic aneurysms, each site made every effort to recruit all eligible patients, as evidenced by the large number of total enrollees. Unfortunately, GenTAC did not include funding for genotyping; however, any participants whose clinical genetic testing identified mutations in genes other than fibrillin 1 would have had their diagnosis changed from MFS to the appropriate alternative diagnosis. Furthermore, the GenTAC Phenotyping Core Laboratory at Johns Hopkins University provided standardization and validation of diagnoses. Fibrillin-1 mutations were documented in 16 ever-pregnant and 11 never-pregnant women in the present study.

Conclusions

Pregnancy in women with MFS is associated with an 8-fold increase in risk of aortic dissection, both types A and B, particularly in the postpartum period. The current data support a recommendation for general cardiac checkup with echocardiographic assessments of the aortic root and ascending aorta before planned pregnancy or during unplanned pregnancy. Our findings also suggest that peripartum ultrasound imaging should additionally include the descending thoracic aorta, although evidence that aneurysmal dilatation precedes type B dissection is lacking. Lack of knowledge of underlying MFS contributes to the risk of aortic complications during pregnancy. These findings underscore the need for early diagnosis, prepregnancy risk counseling, and multidisciplinary periartum management.

Appendix

GenTAC Investigators

Johns Hopkins University: Williams Ravekes, MD, Harry C. Dietz, MD, PhD, Jennifer Habashi, MD. University of Texas–Houston: Dianna M. Milewicz, MD, PhD, Siddharth K. Prakash, MD, PhD. Baylor College of Medicine: Scott A. LeMaire, MD, Shaine A. Morris, MD. Oregon Health & Science University: Kathryn W. Holmes, MD, Cheryl L. Maslen, PhD, Howard K. Song, MD, PhD, G. Michael Silberbach, MD. University of Pennsylvania: Reed E. Pyeritz, MD, PhD, Joseph E. Bavaria, MD, Karianna Milewski, MD, PhD. Weill Cornell Medical College: Richard B. Devereux, MD, Mary J. Roman, MD, Jonathan W. Weinsaft, MD. The Queen's Medical Center: Ralph Shohet, MD. National Institute on Aging: Nazli McDonnell, MD. MedStar Health Research Institute: Federico M. Asch, MD. University of Michigan: Kim A. Eagle, MD. National Heart, Lung, and Blood Institute: H. Eser Tolunay, PhD, Patrice Desvigne-Nickens, MD. National Institute of Arthritis, Musculoskeletal and Skin Diseases: Hung Tseng, PhD. RTI International: Barbara L. Kroner, PhD.

Sources of Funding

The GenTAC Registry has been supported by US federal government contracts HHSN268200648199C and HHSN268201000048C from the National Heart, Lung and Blood Institute and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (Bethesda, MD).

Disclosures

Eagle, MD, reports modest compensation from WL Gore & Associates, Medtronic, and Terumo. LeMaire, MD, reports minor compensation from Baxter Healthcare, Medtronic, Vascutek Terumo, GlaxoSmithKline, Edwards, Cook, and WL Gore & Associates. The remaining authors have no disclosures to report.

References

1. Pyeritz RE. Maternal and fetal complications of pregnancy in the Marfan syndrome. *Am J Med*. 1981;71:784–790.
2. Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr, Eagle KA, Hermann LK, Isselbacher EM, Kazerooni EA, Kouchoukos NT, Lytle BW, Milewicz DM, Reich DL, Sen S, Shinn JA, Svensson LG, Williams DM. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with thoracic aortic disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Circulation*. 2010;121:e266–e369.
3. The Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology. ESC guidelines on the management of cardiovascular disease during pregnancy. *Eur Heart J*. 2011;32:3147–3197.
4. Meijboom LJ, Vos FE, Timmermans J, Boers GH, Zwinderman AH, Mulder BJM. Pregnancy and aortic root growth in the Marfan syndrome: a prospective study. *Eur Heart J*. 2005;26:914–920.
5. Donnelly RT, Pinto NM, Kocolas I, Yetman AT. The immediate and long-term impact of pregnancy on aortic growth rate and mortality in women with Marfan syndrome. *J Am Coll Cardiol*. 2012;60:224–229.
6. Eagle KA; for the GenTAC Consortium. Rationale and design of the national registry of genetically triggered thoracic aortic aneurysms and cardiovascular conditions. *Am Heart J*. 2009;157:319–326.
7. Kroner BL, Tolunay HE, Basson CT, Pyeritz RE, Holmes K, Maslen CL, Milewicz DM, LeMaire SA, Hendershot T, Desvigne-Nickens P, Devereux RB, Dietz HC, Song H, Ringer D, Mitchell M, Weinsaft JW, Ravekes W, Menashe V, Eagle KA; for the GenTAC Registry Consortium. The national registry of genetically triggered thoracic aortic aneurysms and cardiovascular conditions (GenTAC): results from phase I and scientific opportunities in phase II. *Am Heart J*. 2011;162:627–632.
8. Howard DPJ, Banerjee A, Fairhead JF, Perkins J, Silver LE, Rothwell PM; on behalf of the Oxford Vascular Study. Population-based study of incidence and outcome of acute aortic dissection and premorbid risk factor control: 10-year results from the Oxford Vascular Study. *Circulation*. 2013;127:2031–2037.
9. Pacini D, Di Marco L, Fortuna D, Belotti LMB, Gabieri D, Zuss C, Pigini F, Contini A, Barattoni MC, De Palma R, Di Bartolomeo R. Acute aortic dissection: epidemiology and outcomes. *Int J Cardiol*. 2013;167:2806–2812.
10. Omnes S, Jondeau G, Detaint D, Dumont A, Yazbeck C, Guglielminotti J, Luton D, Azria E. Pregnancy outcomes among women with Marfan syndrome. *Int J Gynaecol Obstet*. 2013;122:219–223.
11. Husebye KO, Wolff HJ, Freidman LL. Aortic dissection in pregnancy: a case of Marfan's syndrome. *Am Heart J*. 1958;55:662–676.
12. Sutinen S, Piiroinen O. Marfan syndrome, pregnancy, and fatal dissection of aorta. *Acta Obstet Gynecol Scand*. 1971;50:295–300.
13. Santucci JJ, Katz S, Pogo GJ, Boxer R. Peripartum acute myocardial infarction in Marfan's syndrome. *Am Heart J*. 1994;127:1404–1407.
14. Rosenblum NG, Grossman AR, Gabbe SG, Mennuti MT, Cohen AW. Failure of serial echocardiographic studies to predict aortic dissection in a pregnant patient with Marfan's syndrome. *Am J Obstet Gynecol*. 1983;146:470–471.
15. Donaldson LB, De Alvarez RR. The Marfan syndrome and pregnancy. *Am J Obstet Gynecol*. 1965;92:629–641.
16. Mor-Yosef S, Younis J, Granat M, Kedari A, Milgater A, Schenker JG. Marfan's syndrome in pregnancy. *Obstet Gynecol Surv*. 1988;43:382–385.
17. Rahman J, Rahman FZ, Rahman W, Al-Suleiman SA, Rahman MS. Obstetric and gynecologic complications in women with Marfan syndrome. *J Reprod Med*. 2003;48:723–728.
18. Loeys BL, Dietz HC, Braverman AC, Callewaert BL, De Backer J, Devereux RB, Hilhorst-Hofstee Y, Jondeau G, Faivre L, Milewicz DM, Pyeritz RE, Sponseller PD, Wordsworth P, De Paepe AM. The revised Ghent nosology for the Marfan syndrome. *J Med Genet*. 2010;47:476–485.
19. Rossiter JP, Repke JT, Morales AJ, Murphy EA, Pyeritz RE. A prospective longitudinal evaluation of pregnancy in the Marfan syndrome. *Am J Obstet Gynecol*. 1995;173:1599–1606.
20. Lipscomb KJ, Smith JC, Clarke B, Harris R. Outcome of pregnancy in women with Marfan's syndrome. *Br J Obstet Gynaecol*. 1997;104:201–206.
21. Lind J, Wallenburg HCS. The Marfan syndrome and pregnancy: a retrospective study in a Dutch population. *Eur J Obstet Gynecol Reprod Biol*. 2001;98:28–35.
22. Pacini L, Digne F, Boumendil A, Muti C, Detaint D, Boileau C, Jondeau G. Maternal complication of pregnancy in Marfan syndrome. *Int J Cardiol*. 2009;136:156–161.
23. Mimoun L, Detaint D, Hamroun D. Dissection in Marfan syndrome: the importance of the descending aorta. *Eur Heart J*. 2011;32:443–449.
24. Schoenhoff FS, Jungi S, Czerny M, Roost E, Reineke D, Matyas G, Steinman B, Schmidli J, Kadner A, Carrel T. Acute aortic dissection determines the fate of initially untreated aortic segments in the Marfan syndrome. *Circulation*. 2013;127:1569–1575.
25. Curry RA, Gelson E, Swan L, Dob D, Babu-Narayan SV, Gatzoulis MA, Steer PJ, Johnson MR. Marfan syndrome and pregnancy: maternal and neonatal outcomes. *Br J Obstet Gynaecol*. 2014;121:610–617.