Pregnancy and Marfan Syndrome
An Ongoing Discussion*

Barbara J. M. Mulder, MD, PhD†
Lilian J. Meijboom, MD, PhD‡
Amsterdam and Utrecht, the Netherlands

Pregnancy in patients with Marfan syndrome remains a controversial subject. The 2010 thoracic aortic disease guidelines advocate avoidance of pregnancy if the aortic root diameter exceeds 40 mm and recommend prophylactic aortic root replacement in those who desire pregnancy (1). However, they are not entirely in line with the European and Canadian guidelines, which report an aortic root diameter of <45 mm to be considered safe (2,3). This discrepancy in guidelines is caused by a lack of sufficient studies in the current literature. Only 2 prospective studies have been performed to assess the impact of pregnancy on aortic growth and aortic complications in women with Marfan syndrome (4,5).

Therefore, the new prospective study of Donnelly et al. in 98 women with Marfan syndrome is very interesting (6). The aim of this study was to assess the impact of pregnancy on the rate of aortic growth as well as on short- and long-term clinical outcomes. Of the 98 women, 69 women had 199 pregnancies, and 35 women with 55 pregnancies could be followed prospectively during their pregnancy with multiple cardiac echoes, of which 14 entered pregnancy with an aortic root diameter >40 mm (range 40 to 51 mm).

Data on 2 clinical outcomes were recorded: 1) a composite adverse outcome, defined as death, aortic dissection, or severe symptomatic aortic regurgitation necessitating urgent surgery; and 2) the need for elective aortic surgery during the period of clinical follow-up.

Of the 199 pregnancies there were 170 live births, 26 spontaneous abortions, and 2 ectopic pregnancies. The number of pregnancies ranged from 1 to even 12 (median 3).

No acute aortic dissections were observed during all pregnancies. Two women developed symptomatic carotid artery dissections and 1 patient showed worsening of aortic regurgitation from mild to severe at 38 weeks' gestation with a 49-mm aortic root, necessitating aortic root replacement at 6 months post-partum.

There was a significantly higher rate of aortic growth documented during pregnancy compared with each woman's prior baseline aortic growth rate. The prevalence of both adverse outcome and elective aortic surgery during long-term follow-up was higher in those women who had a prior pregnancy compared with the matched childless group. On multivariate analyses, initial aortic root diameter and rate of change in aortic diameter (log) were the only independent predictors of long-term adverse cardiovascular outcome.

Many case reports and retrospective studies have been published about aortic dissection during or immediately following pregnancy in women with Marfan syndrome (7,8). In these studies, however, there is a large selection bias because many of these women were unknown with Marfan syndrome at the time of pregnancy and therefore preconception aortic diameters are lacking. A great deal is to be gained if health providers caring for women at childbearing age recognize women with Marfan syndrome. Screening programs by a multidisciplinary team should therefore be easily accessible.

If we combine the only 3 prospective studies in the current literature, no type A dissections were reported during 145 pregnancies in 78 nonoperated women with Marfan syndrome. During 29 pregnancies 25 women had an aortic root diameter ≥40 mm (range 40 to 51 mm) (4,5,6). However, there were 4 major cardiovascular complications; 1 type B dissection, 2 carotid artery dissections, and 1 patient who experienced worsening of aortic regurgitation from mild to severe.

For women who had aortic root replacement before pregnancy there are even less prospective data available. In the 3 prospective studies there were only 5 women with a previous aortic root replacement throughout 6 pregnancies. Three women had an elective aortic root replacement (2 valve-sparing and 1 Bentall) and 2 women had a emergency root replacement for type A dissection (Bentall) limited to the ascending aorta. Both women with a limited type A dissection developed type B dissection during pregnancy and in both women with a valve sparing operation, pregnancy was complicated by progressive aortic regurgitation.

In unoperated patients with Marfan syndrome, natural aortic growth and aneurysm formation have been studied in children and adults (9,10). Rapid aortic growth may occur in a small subset of patients (men 15% and women 11%) and has been shown to be a risk factor for aortic dissection (9). Initial aortic diameter, a distensibility <3 × 10⁻³ mm Hg⁻¹ in the thoracic descending aorta (11), previous aortic root replacement, hypertension, and aortic regurgitation have

*Editorials published in the Journal of the American College of Cardiology reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

From the 1Department of Cardiology, Academic Medical Centre, Amsterdam, the Netherlands; and the 2Department of Radiology, University Medical Centre Utrecht, Utrecht, the Netherlands. Both authors have reported that they have no relationships relevant to the contents of this paper to disclose.
been identified as predictors for rapid aortic growth (12,13). Growth of the aortic root is a normal phenomenon in healthy women during pregnancy. The maximum diameter is reached during the third trimester; but still 6 weeks post-partum the diameter remains enlarged by an average of 1 mm (14). The study of Donnelly et al. (6) is the first prospective study to show a significant increase in aortic growth in women with Marfan syndrome during pregnancy compared to baseline. Compared with the other 2 prospective studies (4,5) this patient cohort was larger and had a greater number of pregnancies per woman (mean 3 vs. 2 pregnancies in the studies of Meijboom et al. [5] and Rossiter et al. [4], respectively). Moreover, there might have been a different strategy in the use of beta-blockers, although the overall use of beta-blockers was rather low in all 3 studies (between 30% end 40% to some extent). Although the influence of pregnancy on aortic root growth was significant, the quantitative effects are still small (0.7 to 3 mm per pregnancy).

Not much is known about the long-term effect of pregnancy on the cardiovascular status of women with Marfan syndrome. In the study of Donnelly et al. (6), women with a prior pregnancy had a significantly worse outcome and more often elective surgery during long-term follow up (6). This was in agreement with our study where pregnancy appeared to have a small but significant influence on long-term aortic root growth in women with an aortic root diameter ≥40 mm (5). In clinical practice this would mean an average aortic root growth of 7 mm versus 3 mm in 20 years.

In conclusion, women with Marfan syndrome without previous cardiac complications seem to tolerate pregnancy well, up to an aortic root diameter of 45 mm, with good clinical care before, during, and after pregnancy. Pregnancy should be discouraged in women with previous aortic dissection because of the high risk for aortic complications. Pregnancy causes a slight increase in aortic root diameter. In the long run women with enlarged aortic root diameters at pregnancy, show a slightly accelerated aortic root growth and therefore will have elective aortic root surgery at a younger age. In all women, especially with enlarged aortic root diameters, the pros and cons of pregnancy should be fully discussed as well as the alternatives (childlessness, adoption, and surrogate pregnancy).

REFERENCES


Key Words: aorta ■ Marfan syndrome ■ pregnancy.