

# Increased maternal cardiovascular mortality associated with pregnancy in women with Turner syndrome

Practice Committee of the American Society for Reproductive Medicine

American Society for Reproductive Medicine, Birmingham, Alabama

In women with Turner syndrome, the risk of death from aortic dissection or rupture during pregnancy may be 2%, and this risk persists during the postpartum period owing to pregnancy-related aortic changes. Turner syndrome is a relative contraindication for pregnancy; however, it is an absolute contraindication for pregnancy in a patient with a documented cardiac anomaly. This document replaces the 2008 document of the same name. (Fertil Steril® 2012; ■: ■-■. ©2012 by American Society for Reproductive Medicine.)

## REVIEW METHODS

To evaluate the impact of Turner syndrome on pregnancy outcomes after oocyte donation, a search of Medline from 1950 to January 2011 was performed. We used combinations of medical subject headings “Turner syndrome,” “oocyte donation,” “pregnancy,” “complications,” “cardiovascular,” and “screening.” The reference lists of relevant articles were reviewed for further reports. Only English-language articles were selected, and the search was restricted to published articles. Review articles were included. The relevance of included articles was assessed by one committee member, with subsequent consultation by the committee as a whole. Because the majority of the studies were case series and reviews, methods of aggregation and analysis were limited to tabulation and summarization. The document was revised by the Practice Committee on several occasions.

## DISCUSSION

Turner syndrome results from the partial or complete loss of an X chromosome, with or without cell-line mosaicism, and is defined phenotypically as

patients with short stature, primary amenorrhea, and other characteristics of variable penetrance, including cardiac, skeletal, and renal malformations. The prevalence is 1 in 2,000 live-born girls (1), with 5%–50% exhibiting cardiovascular malformations and 1 in 40 dying of aortic dissection by the age of 85 years (2–4).

Oocyte donation offers women with Turner syndrome the opportunity to achieve pregnancy. However, the increased cardiovascular demands of pregnancy may pose unique and serious risks for these women (5–7). Whereas the risk of maternal death in the general population is approximately 1/10,000, the risk of death during the perinatal period from aortic dissection or rupture in women with Turner syndrome is approximately 2% (8–10). When evaluating pregnancy outcomes in patients with Turner syndrome, distinction is not made between a “pure” 45,X karyotype and a mosaic pattern, and therefore all Turner syndrome patients should be considered to be at risk (9, 11, 12).

We do not have sufficient information to determine whether people with

gonadal digenesis without Turner phenotype are at increased risk. Women with Turner syndrome at greatest risk of aortic dissection and rupture include those exhibiting baseline or progressive aortic root dilation, bicuspid aortic valve, coarctation of the aorta with or without prior surgical repair, and hypertension (6, 7). However, aortic dissection may also occur in the absence of known risk factors and at an aortic diameter of <4 cm (13). Prompt recognition of dissection may provide the opportunity for successful surgical intervention in some, though not all, women. Some institutions use transesophageal echocardiography instead of magnetic resonance imaging (MRI).

Women with Turner syndrome expressing interest in oocyte donation should be carefully evaluated with both echocardiography and MRI, preferably by a cardiologist with expertise in adult congenital heart disease. Aortic diameter may not be an appropriate predictor of risk in women with Turner syndrome, because of their small stature and body surface area. Therefore aortic size measured by MRI should be adjusted for body surface area and reported as the aortic size index (ASI). An ASI >2.0 cm/m<sup>2</sup> identifies those patients at a particularly increased risk for dissection (13). In a group of 166 women with Turner syndrome with a mean age of 36 years and followed

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Correspondence to Practice Committee, American Society for Reproductive Medicine, 1209 Montgomery Hwy., Birmingham, AL 35216 (E-mail: [asrm@asrm.org](mailto:asrm@asrm.org)).

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for a mean of 3 years, 33% of the women with ASI  $>2.5$  cm/m<sup>2</sup> experienced aortic dissection (13). Any risk factor or significant abnormality found on imaging is best regarded as a contraindication to pregnancy. Even those having a normal evaluation should be thoroughly counseled regarding the risk of cardiac complications and death during pregnancy, because aortic dissection may still occur. Indeed, approximately one-half of aortic dissections occur in the third trimester or postpartum (8). Patients should be counseled that pregnancy carries not only a risk of maternal death, but also a potentially increased risk of premature death in the months and years after delivery because of pregnancy-related aortic dilation or not yet identified changes of the vessel wall (14, 15). All patients should be offered surrogacy and adoption as alternatives for having a family.

Those with normal evaluations who choose to proceed with donor oocyte require careful observation and frequent reevaluation during pregnancy (9, 16, 17). Specific recommendations for surveillance in women with Turner syndrome during pregnancy include: 1) treatment of hypertension; 2) periodic echocardiography or MRI and consultation with a cardiologist; 3) women in stable condition having an ascending ASI  $<2$  cm/m<sup>2</sup> may attempt vaginal delivery under epidural anesthesia; and 4) women exhibiting baseline or progressive aortic root dilation should have an elective cesarean delivery under epidural anesthesia before the onset of labor. In those patients who choose to proceed with ART, elective single-embryo transfer should be preferred, because multiple gestation increases the risks of perinatal complications (9). In addition, the obstetrician should be aware that complications such as preeclampsia and gestational diabetes also occur with increased frequency in pregnant patients with Turner syndrome.

For Turner syndrome patients who achieved pregnancy with donor oocytes, one study found reported that approximately 40% had no complications, 40% had pregnancy-associated hypertension, and the remainder had a range of significant morbidities including aortic rupture, gestational diabetes mellitus, eclampsia, and acute liver failure (9). It is worth noting that in this study only 37.6% of the patients were prescreened with echocardiography or thoracic MRI. Four-fifths of these women had a cesarean section, and one in twelve had postpartum hemorrhage. Approximately 40% of the infants were born prematurely and had a mean birth weight of 2,599 g (9).

## SUMMARY

The risk of death during pregnancy from aortic dissection and rupture may be 2% or higher for women with Turner syndrome. In addition, pregnancy-related changes to the aorta may increase the risk of aortic dissection, aortic rupture, and premature death in subsequent years.

## CONCLUSIONS

- Turner syndrome is a relative contraindication for pregnancy, and patients should be encouraged to consider alternatives, such as gestational surrogacy or adoption.

- Cardiology and maternal-fetal medicine consultation for evaluation and careful screening are required before considering pregnancy by oocyte donation.
- Cardiac MRI revealing any significant abnormality and/or ASI  $>2$  cm/m<sup>2</sup> represents an absolute contraindication for attempting pregnancy in a woman with Turner syndrome.
- Women with Turner syndrome having a normal cardiac MRI and evaluation who decide to attempt pregnancy after thorough counseling are still at much higher risk for associated morbidity and mortality and require careful observation and frequent formal reevaluation throughout gestation and postpartum.

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The following members of the ASRM Practice Committee participated in the development of this document. All committee members disclosed commercial and financial relationships with manufacturers or distributors of goods or services used to treat patients. Members of the committee who were found to have conflicts of interest based on the disclosed relationships did not participate in the discussion or development of this document.

Samantha Pfeifer, M.D.; R. Dale McClure, M.D.; William Catherino, M.D., Ph.D.; Marcelle Cedars, M.D.; John Collins, M.D.; Owen Davis, M.D.; Jeffery Goldberg, M.D.; Michael Thomas, M.D.; Catherine Racowsky, Ph.D.; Eric Widra, M.D.; Mark Licht, M.D.; Clarisa Gracia, M.D.; Robert Rebar, M.D.; Andrew La Barbera, Ph.D.

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