Maternal cardiovascular morbidity and mortality associated with pregnancy in individuals with Turner syndrome: a committee opinion

The Practice Committee of the American Society for Reproductive Medicine

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In individuals with Turner syndrome, the risk of death from aortic dissection or rupture during pregnancy may be as high as 1%, and it is unclear whether 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 an aortic size index of >2.5 cm/m^2 or an aortic size index of ≥ 2.0 cm/m^2 with a documented cardiac anomaly or other risk factors. This document replaces the 2012 document of the same name. (Fertil Steril® 2024;122:612–21. ©2024 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Practice committee, Turner syndrome, ASRM, maternal cardiovascular morbidity, mortality

A REVIEW OF THE LITERATURE

To evaluate the impact of Turner syndrome on pregnancy outcomes, a search of Medline from 1990 to April 2023 was performed. We used combinations of medical subject headings ''Turner syndrome,'' ''oocyte donation,'' ''pregnancy,'' ''complications,'' ''cardiovascular,'' ''aortic dissection,'' and ''screening.'' The reference lists of relevant articles were reviewed for further reports. Because most studies were case series and reviews, methods of aggregation and analysis were limited to tabulation and summarization.

Turner syndrome (TS) results from the partial or complete loss of an X chromosome, with or without cell-line mosaicism, and is characterized by clinical features, including short stature and primary amenorrhea. Other features, including cardiac, skeletal, and renal malformations, have variable penetrance. Turner syndrome is the most common sex chromosome abnormality among women; the reported prevalence ranges from 17–64 per 100,000 female live births (LBs) (1–7). Biobank studies have reported rates as high as 88 per 100,000 female LBs, likely reflecting the inclusion of very low-level mosaicism that would not be captured on a standard karyotype (8).

Overall mortality for individuals with TS is three times higher than the general population (9), with cardiovascular complications cited as the major cause of death according to the American Heart Association (1, 9–13). Congenital heart malformations occur in 23%–50% of individuals with TS, with a higher incidence in those with 45,X karyotypes compared with 45,X/46,XX mosaicism, or other structural abnormalities (14–18). The most common congenital heart defects include bicuspid aortic valve, coarctation of the aorta, and thoracic aortic aneurysm, with each attributing varying risks for aortic dissection. Unfortunately, many of these abnormalities go undetected until complications occur, and thus, likely contribute to the higher rates of morbidity and mortality seen in this population (19). Although the severity of aortic dilation is highest in individuals with TS with the congenital abnormalities mentioned above, some degree of dilation may be also present in those with normal valve function and blood pressure (13, 20, 21). Compared with the general female population, the risks of aortic aneurysm formation, dissection, and rupture are increased 100-fold in patients with TS (19). Furthermore, the average age of individuals with TS experiencing aortic dissection is 35 years, and by the age of 85 years, 1 in 40 individuals with TS will die from aortic dissection (9, 22).

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PREGNANCY AND ASSOCIATED RISKS

Most individuals with TS are infertile secondary to early and progressive gonadal dysgenesis resulting in primary ovarian insufficiency. However, both unassisted pregnancy and pregnancy achieved using assisted reproductive technologies (ARTs) therapy using donor oocytes (and rarely autologous oocytes) have been reported, and span across patients with TS with a range of karyotypes. Previously, it was believed that conception with autologous oocytes was limited to those with mosaic karyotypes containing a 46,XX cell line, and oocyte donation was the only option available for 45,X (not mosaic) individuals. However, there are several documented cases of 45,X individuals having multiple unassisted pregnancies (23–26). Furthermore, recent investigations report rates of unassisted pregnancy of approximately 3%–8%, with a few single-center studies reporting unassisted pregnancy and LB rates as high as 13.5% and 7.6%–11.5%, respectively (1, 19, 27–29). To date, 244 unassisted pregnancies in individuals with TS have been reported (Table 1).

These data represent compiled events from case series and case reports published to date (individual study information is detailed in Tables 2 (24, 27–38) and 3 (21, 39–42)). When cases were reported separately in a case report and later in a case series, the case was only counted once.

Although most individuals will need donor oocytes to conceive, oocyte cryopreservation (OC) and ovarian tissue cryopreservation (OTC) are available techniques to preserve fertility using autologous oocytes. Oocyte cryopreservation is reserved for those who have completed puberty, with the first LB after OC in an individual with TS reported in 2022 (43). Ovarian tissue cryopreservation remains the only option for prepubertal individuals or those who cannot safely tolerate ovarian hyperstimulation. Although >185 LBs have been reported in other populations using OTC for malignancy or other gonadotoxic treatment, there have been no reported births in individuals with TS (44, 45). One study that described 73 individuals with TS (1–12 years: n = 24 [33%]; 13–17 years: n = 42 [58%]; and 18–27 years: n = 7 [10%]) planning OTC showed that follicles were present in only 21% of patients, although these data were lacking in 22% of cases (46). Of these 73, only two patients have had their ovarian tissue reimplanted, and neither has regained endocrine function (46). There has been one reported pregnancy in a patient with mosaic TS who cryopreserved ovarian tissue at the age of 15 years in the setting of antimüllerian hormone levels of 0.3 ng/mL. Subsequent transplantation at age 24 years resulted in an unassisted pregnancy, which ended in miscarriage. Patients should be counseled that OTC is an emerging technique in this population, and there are concerns that it will be less effective in patients with TS with diminished ovarian reserve (47). For most individuals with TS, oocyte donation offers the best opportunity to achieve pregnancy.

No matter the method used to conceive, the increased cardiovascular demands of pregnancy may pose unique and serious risks for individuals with TS (19, 48–50). Common pregnancy pathologies, such as preeclampsia, may be particularly harmful to individuals with TS by directly promoting vascular damage and facilitating aneurysm formation (19). Patients with TS 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 (13, 49, 50). However, aortic dissection may also occur in the absence of known risk factors and an aortic diameter of <4 cm (11, 51).

There is evidence that the risk for adverse pregnancy outcomes may differ among individuals who conceive without assistance and those who use oocyte donation (52). To date, no maternal deaths have been reported among individuals with TS who have achieved unassisted pregnancies (19). Two cases of aortic dissection have been reported: one in an individual in her second unassisted pregnancy, not previously known to have TS, who delivered a healthy infant via cesarean section (53), and a second individual with a mosaic karyotype who experienced dissection in the postpartum period (21). The risk of severe hypertensive disorders during pregnancy also appears to be low in these individuals (24, 35). In contrast, case reports of patients experiencing severe cardiovascular complications after conceiving with donor oocytes began appearing in the literature before 2000, with more recent publications also reporting high rates of pregnancy-related hypertension associated with preterm delivery and infants with low birth weight (52). Table 1 summarizes the total number of pregnancies, the total number of pregnancies complicated by hypertensive disorders of pregnancy, aortic dissections, and maternal deaths among patients with TS.

There are several proposed explanations for the discrepancy in the prevalence of pregnancy-related hypertension

TABLE 1

Pregnancy and cardiovascular outcomes in individuals with Turner syndrome.

Mode of conception	Pregnancies (n)	HTN disorders of pregnancy (n)	Aortic dissection (n)	Maternal deaths (n)
Unassisted	244	9	2	0
ART therapy with donor oocytes	405	122	10	8
Unspecified	189	24	0	0
Total n (% of all pregnancies)	838	155 (18.5)	12 (1.4)	8 (0.95)

Note: ART = assisted reproductive technology; HTN = hypertension.

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TABLE 2

Summary of cohort studies reporting pregnancy outcomes in individuals with Turner syndrome.

Reference	Type of Study	Total pregnancies(Time period)	Karyotype(n)	Mode of conception	Total live births(n)	Cardiac anomalies(n)	HTN disorders of pregnancy(n)	Aortic dissection(n)	Deaths(n)
Cauldwell et al. (29) (2022)	Retrospective multicenter cohort	127 (2000–2020)	(81 individuals) 45,X: 24 45,X/46,XX: 38 Other: 13 Unknown: 6	Unassisted: 73 IVF, DO: 54	105	11 (BAV) 5 (CoA) 3 had aortic root replacement before pregnancy	GHTN: 11 PreE: 20	2	1
Calanchini et al. (27) (2020)	Retrospective single-center cohort	Not provided (1975–2019)	(of individuals achieving pregnancy) 45X: 5 45,X/46,XX; 45,X/47,XXX; or 45,X/46,XX/47,XXX: 11 Any Y chromosome material: 2 Other: 6 Unknown: 4	Unassisted: 37 IVF, DO: 9	46	4 (BAV) 1 (APVD) 1 (BAV + CoA) 1 (BAV + CoA + ASD + VSD)	PreE: 2	0	0
Andre et al. (30) (2019)[a]	Retrospective multicenter cohort	39 (2012–2016)	(73 individuals) 45,X: 28 45,X/46,XX: 8 46,X,del(X): 6 Others: 17 Unknown: 14	IVF, DO	24	Not reported	GTH: 11 PreE: 6 (2 necessitating delivery at 23 and 18 wks)	0	1 (status epilepticus at 21 wks)
Cadoret et al. (31) (2018)[b]	Retrospective multicenter cohort	– (2006–2017)	Unclear: DO were used in 45,X, and 71% of unassisted had 45,X/46,XX	Unassisted: 22 IVF, OD: 62	84	11 (BAV)	GHTN: 12 PreE: 5	0	0
Bernard et al. (32) (2016)	Retrospective multicenter cohort	52 (1999–2014)	(27 individuals) 45,X: 2 45,X/46XX: 19 Y chromosome: 1 Ring: 2 Isochromosome: 1 Other: 2	Unassisted	30	2 (BAV) 1 (CoA)	GHTN: 2 PreE: 2	0	0
Doğer et al. (33) (2015)	Retrospective single-center cohort	52 (2009–2013)	(16 individuals) 45,X/46,XX: 35 45,X/46,XX/47,XXX: 17	Unassisted: 11 IVF, AO: 5	17	Not reported	Not reported	Not reported	Not reported
Hagman et al. (34) (2013)	Retrospective multicenter cohort	106 (1992–2011)	(100/106 individuals) 45,X: 44 45,X/46,XX: 16 Other: 40	IVF, DO	131	10	GHTN: 12 PreE: 24 Eclampsia: 5	1	0

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TABLE 2

Continued.

Reference	Type of Study	Total pregnancies(Time period)	Karyotype(n)	Mode of conception	Total live births(n)	Cardiac anomalies(n)	HTN disorders of pregnancy(n)	Aortic dissection(n)	Deaths(n)
Bryman et al. (35) (2011)	Retrospective multicenter cohort	124 (1993–2011)	(57 individuals) 45,X:17 45,X/46,XX: 27 Karyotype with any Y: 4 Isochromosome, ring, trisomy x: 9	Unassisted: 23 IVF, AO: 3 IVF, DO: 30 IUI: 1	67	1 (CoA) [a]Only reported on cases with aortic dissection	3	1	0
Chevalier et al. (36) (2011)[a]	Retrospective multicenter cohort	93 (1991–2009)	(72/82 individuals) 45,X: 32 45,X/46,XX: 23 Other: 15 Y mosaicism: 2	IVF, DO	81	1 (CoA) 5 (BAV)	GHTN: 14 PreE: 13 HELLP syndrome: 1 Eclampsia: 3	2	2
Hadnott et al. (24) (2011)	Retrospective single-center cohort	13 (2001–2010)	(10 individuals) 45,X: 6 45,X/47,XXX: 1 Others: 3	Unassisted: 5 ART therapy: 5	14	2 (BAV)	PreE: 1	0	0
Mercadal et al. (37) (2011)	Retrospective single-center cohort	18 (1992–2011)	(14 individuals) 45,X: 8 45,X/46,XX: 0 45,X/47,XXX: 1 45,X/Y: 2 Other: 3	IVF, DO	10	1 (CoA)	GHTN: 1 PreE: 4	0	0
Bodri et al. (38) (2006)	Retrospective single center cohort	17 (2001–2004)	(21 individuals) 45,X: 13 Other: 8	IVF, DO	8	1 (aortic insufficiency)	GHTN: 2 PreE: 3	0	0
Birkebaek et al. (28) (2002)	Retrospective multicenter cohort	61 (1973–1993)	(33 individuals) 45,X: 1 45,X/46,XX: 27 46,XX/structural abnormality of second X: 5	Unassisted: 59 IVF, DO: 2	64	Not reported	Not reported	Not reported	Not reported

Note: AO = autologous oocyte; APVD = anomalous pulmonary venous drainage; ART = assisted reproductive technology; AST = atrial septal defect; BAV = bicuspid aortic valve; CoA = coarctation of the aorta; DO = donor oocytes; GHTN = gestational hypertension; HTN = hypertension; IUI = intrauterine insemination; IVF = in vitro fertilization; OD = oocyte donation; PreE = preeclampsia; VSD = ventricular septal defect.

[a] Same centers, but different time periods.

[b] Overlaps data with Chevalier et al. (36). Tabulated values represent nonduplicated data only.

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between individuals with TS who conceive naturally and those who use donor oocytes. All individuals using donor oocytes to achieve pregnancy are at a higher risk of pregnancy-induced hypertension. It has been suggested that the hormonal treatment and environment necessary for uterine preparation for implantation and pregnancy maintenance may cause dysfunctional or abnormal vascular remodeling (54). This abnormal response may be even higher in those with TS because of intrinsic preexisting vascular dysfunction and hypertension. Additionally, compared with those with TS requiring donor oocytes, individuals with unassisted pregnancies are, on average, younger and more likely to have mosaic cell lines containing a 46,XX karyotype that may contribute to their more positive fertility prognosis as well as normal vascular physiology (19). There is likely an unknown population of individuals representing the least severe cases of TS who are never diagnosed. Finally, the underreporting of complications in individuals with unassisted pregnancies in smaller local or rural care centers may also contribute to this discrepancy (19).

Whereas the risk of pregnancy-related death in the general US population is approximately 17.3 deaths per 100,000 LBs, the risk of death during the perinatal period from aortic dissection or rupture in patients with TS has been reported historically to be approximately 2% or 2,000 deaths per 100,000 (36, 55–57). Two widely quoted studies are responsible for this estimate. In 2001, Karnis et al. (56) distributed a survey to 258 programs in the United States investigating experience with donor-oocyte pregnancies in individuals with TS. The response rate was approximately 50%, with data tallying 101 pregnancies, 94 LBs, no deaths, or aortic dissections among treated individuals with TS, and 1 death from aortic rupture in a patient who was awaiting treatment (56). Because only half of the donor-oocyte programs responded to the survey, the investigators estimated that there were likely a total of 200 donor-oocyte pregnancies in individuals with TS during this period, assuming a similar pregnancy rate in the clinics of the nonresponders (19, 56). Because there were 4 reported maternal deaths in the United States from 1997–2001 resulting from aortic dissection in patients with donor-oocyte pregnancies, the investigators used these 4 deaths as the numerator and concluded that the death rate among patients with TS using donor oocytes to conceive was 2% (19, 56). Nearly 10 years later, a French multicenter retrospective study of individuals conceiving after using donor oocytes demonstrated similar findings, reporting 2 maternal deaths in the late third trimester of pregnancy because of aortic dissection or rupture out of 93 total pregnancies (36). Both reports may be limited, the first because of assumptions in calculating mortality rates, and the retrospective series with two reported events may have benefited from a larger sample size.

More recent data, however, have shown more favorable outcomes that may be because of improvements in childhood and prenatal cardiovascular screening. A prospective multicenter cohort study followed 89 nonpregnant individuals with TS for a median follow-up of 3.0 years to assess changes in aortic dilation with time (11). Ascending aortic dilation was seen in 38.2% at baseline and was statistically significantly associated with bicuspid aortic valve, systolic blood pressure, and age (11). Interestingly, aortic diameters were stable during the 3-year follow-up, and no aortic dissections occurred; the investigators concluded that the progression in aortic dilation with time might follow a more benign course than previously suggested (11). Another multicenter retrospective analysis compared cardiovascular outcomes during pregnancy and 6 months postpartum among 60 pregnant individuals with TS compared with age-matched nonpregnant controls with TS (58). In the pregnant group, approximately half were primigravid, half used ART therapy to achieve pregnancy (14/68 pregnancies used donor oocytes; 19/68 pregnancies after autologous oocyte retrieval), 80% had a structurally normal heart, and 25% had a 45,X karyotype (58). There were no cardiovascular events (cardiovascular-related death, aortic dissection/rupture, or aortic intervention) in either group, although 13% of pregnancies were complicated by hypertensive disorders of pregnancy (58). Additionally, fetal outcomes included small for gestational age (18%), preterm delivery (15%), and fetal death secondary to severe preeclampsia (3%) (58). Finally, a large cohort of 276 individuals with TS who were participating in a longitudinal natural history study defined by stringent karyotype analyses and robust clinical evaluations found no difference in aortic diameters when comparing parous individuals ($n = 9$) to nonparous individuals ($n = 88$) and no difference when comparing unassisted individuals ($n = 4$) to those using ART therapy to conceive ($n = 5$) (24). This study included an individual who conceived with twins after ART therapy and had a stable aortic size index (ASI) of 2.4 cm/m^2 after 18 years of follow-up after pregnancy (24). Tables 2 and 3 summarize all reported cases of pregnancy in TS since 1998 (21, 24, 27–29, 30–42). It is important to note that these aggregated data include studies spanning many years and report cases from as early as 1973. With time, patient selection criteria and advancements in cardiac imaging modalities and monitoring have likely contributed to improved patient outcomes. Using all available data, we calculated the overall rates of hypertensive disorders of pregnancy, aortic dissection, and maternal death to be 18.5%, 1.4%, and 0.95% per pregnancy, respectively (Table 1).

It is unclear whether pregnancy in individuals with TS increases cardiovascular morbidity or mortality in subsequent years. One retrospective Swedish population-based registry study compared cardiovascular disease outcomes across three groups: 124 individuals with TS who had given birth between 1973 and 2010 (cases), 378 age-matched patients with TS who had not given birth (the first control group), and 1,230 patients without TS who were matched for maternal age, number of children, and year of birth of the first child (the second control group) (35). Of individuals with TS and a history of childbirth, 20 (16.1%), 35 (28.2%), 14 (11.3%), and 55 (44.4%) had 45,X, 45,X/46,XX mosaic, low-grade mosaic (<6%), and other karyotypes, respectively. In individuals with TS and no history of childbirth, corresponding proportions of karyotypes were 160 (42.3%), 43 (11.4%), 168 (44.4%), and 7 (1.9%), respectively (35). Interestingly, no mortalities occurred in patients with TS who had a previous birth, compared with 14 (3.7%) of those with TS without a previous

TABLE 3

Case reports reporting pregnancy outcomes in individuals with Turner syndrome.

Reference	Type of study	Year	Karyotype	Mode of conception	Total live births (n)	Cardiac anomalies	HTN disorders of pregnancy (n)	Aortic dissection (n)	Maternal death (n)
Garvey et al. (39) (1998)	Case report	1997	Not reported	IVF, DO	1	CoA	PreE	1	1
Nagel and Tesch (40) (1997)	Case report	1997	Not reported	IVF, DO	2	None	GHTN:1	2	2
Beauchesne et al (41) (2001)	Retrospective single-center case series	1980–2000	Not reported	IVF, DO	2 (twins)	BAV, CoA s/p repair	0	1	1
Carlson et al. (21) (2012)	Retrospective registry case series	1988–2010	Not reported	IVF, DO	2 (twins)	BAV	0	1	1
Weytjens et al. (42) (2000)	Case report	2000	45,X/46,XX	Unassisted	1	None	Eclampsia	1	0

Note: APVD = anomalous pulmonary venous drainage; ASD = atrial septal defect; BAV = bicuspid aortic valve; CoA = coarctation of the aorta; DO = donor oocytes; GHTN= gestational hypertension; HTN = hypertension; IVF = in vitro fertilization; PreE = preeclampsia; VSD = ventricular septal defect.

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birth and 9 (0.7%) of those without TS over a median 10-year follow-up period (35). Seven (50%) individuals with TS died of cardiovascular-related conditions, with 5 dying from aortic rupture between the relatively young ages of 25 and 37 years (35). Although the prevalence of aortic aneurysms was slightly higher in the group of patients with TS who had experienced childbirth, there were higher rates of ischemic heart disease, cardiac malformations, and hypertension in the group who had never had children (35). Limitations noted by the investigators included the need for longer follow-up to fully assess these rare events and the fact that individuals who were able to have children likely represent a select population of healthier individuals with TS. A smaller study compared changes in aortic dilation over time among 22 pregnant individuals with TS who had imaging during and after pregnancy compared with 27 matched individuals with TS and no history of pregnancy. After approximately 3 years of follow-up, there was no difference in aortic dilation (0.23 vs. 0.32 mm/y, $P=.686$ for the pregnant vs. nonpregnant group, respectively); there were also no complications during pregnancy or in the first 6 months after delivery (59). Another retrospective case study compared prepregnancy and postpregnancy aortic diameter measurements in 12 parous individuals with TS over an approximately 3-year period and found that the increase in dilation per year was significantly greater than a control group of 70 nulliparous individuals with TS (27). However, this same study found no differences in mortality or the incidence of new diagnoses of comorbidities in individuals who experienced LB compared with nulliparous individuals over a 10-year follow-up period (27).

PREGNANCY EVALUATION AND MANAGEMENT

International consensus groups, as well as subspecialty groups such as the American Heart Association, have published individual guidelines detailing recommendations for individuals with TS who are interested in pursuing pregnancy and/or fertility preservation (13, 60). These guidelines provide recommendations for cardiovascular screening and assessment before pregnancy and cardiovascular monitoring and management during pregnancy. All individuals with TS, irrespective of preexisting history of cardiovascular disease or lack thereof, expressing interest in achieving pregnancy should be thoroughly counseled regarding the risk of cardiac complications and death during pregnancy. These individuals should also be thoroughly counseled on all available options for family building, including adoption and/or the use of a gestational carrier. All individuals with TS attempting pregnancy on their own or pursuing ART therapy should be evaluated with both echocardiography and magnetic resonance imaging (MRI) within 2 years before conception, preferably by a cardiologist with expertise in adult congenital heart disease (13, 60). Aortic diameter may not be an appropriate predictor of risk in individuals with TS, because of their small stature and body surface area. Therefore, the aortic size measured using MRI should be adjusted for body surface area and reported as the ASI. Pregnancy risk stratification is based on the presence of known risk factors for aortic

dissection as well as ASI thresholds (13). Despite the lack of prospective longitudinal studies supporting causation between increasing measures of ASI and the risk of aortic dissection in women with TS, the American Heart Association recommends the use of ascending ASI as the best method to predict absolute aortic size in these patients (13). On the basis of expert opinion, in the absence of other risk factors, an ASI of >2.5 cm/m^2 in individuals aged ≥ 15 years should be regarded as an absolute contraindication to pregnancy (13, 60). A history of previous aortic dissection should be also considered an absolute contraindication to pregnancy (13, 60). Individuals with an ASI of 2.0–2.5 cm/m^2 and other associated risk factors such as bicuspid aortic valve, elongation of the transverse aorta, coarctation of the aorta, or hypertension should be also counseled to avoid pregnancy (13, 60). 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, in a recent study of 81 patients with TS and a history of at least one pregnancy, only 2 cases of aortic dissection occurred in patients with an ASI of 1.5 cm/m^2 and 1.6 cm/m^2, respectively, resulting in one maternal death (29). Importantly, only 54% of these individuals had cardiovascular imaging within the 2 years before conception, and of these individuals, none had an ASI of >2.0 cm/m^2. Patients should be counseled that pregnancy carries a risk of maternal death. It is unclear whether there is an increased risk of premature death in the months and years after delivery because of pregnancy-related aortic dilation or changes in the vessel wall.

All individuals with TS who ultimately conceive require careful observation and frequent reevaluation during pregnancy in specialized centers by a multidisciplinary team with knowledge of TS (13, 36, 61, 62). Specific recommendations for surveillance in individuals with TS during pregnancy include maintaining blood pressure below 135/85 mm Hg; at least one transesophageal echocardiogram during pregnancy in those without aortic dilation or other risk factors; and periodic echocardiography or MRI and consultation with a cardiologist at 4–8-week intervals during pregnancy and in the first month after delivery for those with ASI of >2.0 cm/m^2 or any risk factors (13). Management during pregnancy includes treatment of hypertension using similar recommendations as in those with hypertension without TS and initiation of 75–81 mg of aspirin daily from 12 weeks until delivery for those using donor oocytes (13). Prophylactic aorta repair may be considered in individuals with baseline ASI of >2.5 cm/m^2 and progressive enlargement. In the case of acute dissection, emergency life-saving aortic surgery should be performed; in cases of a viable pregnancy, this should occur immediately after cesarean delivery (13). Recommendations regarding the mode of delivery are stratified also by the severity of the ascending ASI and the presence of risk factors. Patients with TS with an ASI of <2.0 cm/m^2 can consider vaginal delivery. Individuals with an ASI of 2.0–2.5 cm/m^2 can consider either a vaginal delivery with epidural anesthesia and an expedited second stage or a cesarean delivery. For those in the highest risk category for acute aortic dissection, including an ASI of >2.5 cm/m^2 or a history of aortic dissection, a cesarean delivery is recommended (13). In patients who choose to proceed with ART therapy, elective single-embryo transfer is strongly recommended, because multiple gestation increases the risks of perinatal complications (36). Some evidence suggests that individuals with TS who conceive with their own oocytes have higher rates of offspring (or embryos) with sex chromosome abnormalities or other aneuploidy; it may be reasonable to offer preimplantation genetic testing for individuals with TS utilizing ART therapy to conceive or for fertility preservation (63, 64). In addition, the obstetrician should be aware that complications such as preeclampsia and gestational diabetes also occur with increased frequency in pregnant patients with TS (19).

SUMMARY

The risk of death during pregnancy from aortic dissection and rupture may be 1% or higher for individuals with TS. In addition, available data suggest that pregnancy-related changes to the aorta may not increase the risk of aortic dissection, aortic rupture, and premature death in subsequent years. Patients with TS who achieve unassisted pregnancy may be at lower risk of complications, but data are limited.

CONCLUSIONS

- Turner syndrome poses increased risks of morbidity and mortality during pregnancy. In most cases, it is a relative contraindication for pregnancy, and patients should be encouraged to consider alternatives, such as gestational surrogacy or adoption. With certain cardiac anomalies, the presence of TS should be considered an absolute contraindication to pregnancy.
- Individuals with TS who achieve unassisted pregnancy may experience lower rates of complications such as hypertensive disorders of pregnancy and aortic dissection compared to those who achieve pregnancy using donor oocytes, but these complications are still more common than in the general population.
- Cardiology and maternal-fetal medicine consultations for evaluation and careful screening are required before considering pregnancy by oocyte donation.
- Cardiac MRI revealing an ASI of >2.5 cm/m^2 or an ASI of ≥ 2.0 cm/m^2 with any significant abnormality or other risk factor represents an absolute contraindication for attempting pregnancy in an individual with TS on the basis of expert opinion.
- Individuals with TS having a normal cardiac MRI and evaluation and 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.
- Single-embryo transfer is strongly recommended in patients with TS.

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Morbilidad materna cardiovascular y mortalidad asociada al embarazo en mujeres con Síndrome de Turner: opinión del comité.

En individuos con síndrome de Turner, el riesgo de muerte por disección aórtica o ruptura durante el embarazo puede llegar al 1% y no está claro si este riesgo persiste durante el periodo posparto debido a los cambios aórticos relacionados con el embarazo. El síndrome de Turner es una contraindicación relativa para el embarazo; sin embargo, es una contraindicación absoluta para el embarazo en una paciente con un con un índice de tamaño aórtico de $>$2,5 cm/m2 o un índice de tamaño aórtico $\geq$2,0 cm/m2 con una anomalía cardiaca documentada u otros factores de riesgo. Este documento sustituye al documento de 2012 del mismo nombre.