European Journal of Cardio-Thoracic Surgery 58 (2020) 294–301
doi:10.1093/ejcts/ezaa048 Advance Access publication 7 April 2020

ORIGINAL ARTICLE

Cite this article as: Ma W-G, Zhu J-M, Chen Y, Qiao Z-Y, Ge Y-P, Li C-N *et al*. Aortic dissection during pregnancy and postpartum in patients with Marfan syndrome: a 21-year clinical experience in 30 patients. Eur J Cardiothorac Surg 2020;58:294–301.

Aortic dissection during pregnancy and postpartum in patients with Marfan syndrome: a 21-year clinical experience in 30 patients

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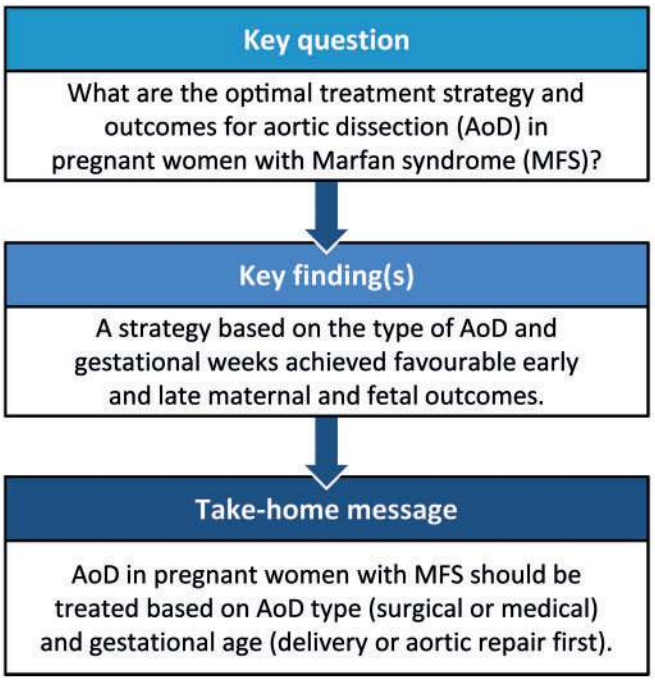
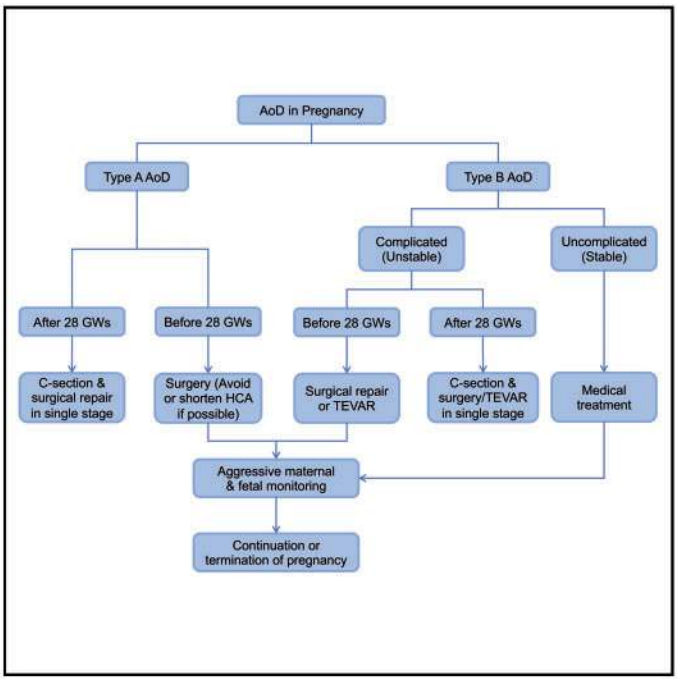
Received 6 October 2019; received in revised form 14 January 2020; accepted 31 January 2020





Abstract

OBJECTIVES: Pregnancy-related aortic dissection (AoD) in Marfan syndrome is a lethal catastrophe. Due to its rarity and limited clinical experience, there is no consensus regarding the optimal management strategy. We seek to present our 21-year experience in such patients , focusing on management strategies and early and late outcomes.

METHODS: Between 1998 and 2019, we managed 30 pregnant women with Marfan syndrome (mean age 30.7 ± 4.3 years) who sustained AoD at a mean of 28.3 ± 8.8 weeks of gestation (GWs). AoD was acute in 21 (70%), type A (TAAD) in 24 (80%) and type B (TBAD) in 6 (20%). Fourteen TAADs (58.3%, 14/24) and 2 TBADs (33.3%, 2/6) occurred in the third trimester or postpartum. The maximal aortic size was < 45 mm in 26.7% (8/30; 3 TAADs, 5 TBADs). Management strategy was based on the types of dissection and GWs (i.e. surgical versus medical treatment, surgery or delivery first).

RESULTS: TAADs were treated medically in 1 and surgically in 23. The timing of delivery and surgery were caesarean first at 35.4 ± 6.1 GWs in 7 (29.2%), followed by surgery after mean 46 days; single-stage C-section and surgery at 32.0 ± 5.0 GWs in 10 (41.7%); and surgery

Presented at the 33rd Annual Meeting of the European Association for Cardio-Thoracic Surgery, Lisbon, Portugal, 3–5 October 2019.

first at 18.0 ± 5.8 GWs in 6 (25%), followed by C-section after 20 days. Maternal and foetal mortality were 28.6% (2/7) and 14.3% (1/7), 10.0% (1/10) and 20.0% (2/10) and 16.7% (1/6) and 83.3% (5/6), respectively. Five TBADs (83.3%) were managed with C-section followed by surgery in 2 and medical treatment in 3. The respective maternal and foetal mortality were 50% (1/2) and 100% (2/2) and 33.3% (1/3) and 33.3% (1/3), respectively. One TBAD was managed surgically first followed by C-section, resulting in maternal survival and foetal death. Follow-up was complete in 95.8% (23/24) at 3.7 ± 2.9 years. Four late deaths occurred and reoperation was performed in 1 patient. Maternal and foetal survival were 64.3% and 54.1% at 6 years, respectively.

CONCLUSIONS: Management of AoD in pregnant women with Marfan syndrome should be based on types of dissection (surgical versus medical) and gestational age (delivery or surgery first), which largely determine maternal and foetal survival. Aortic repair should be considered prior to conception in women with Marfan syndrome even at diameters smaller than recommended by current guidelines.

Keywords: Aortic aneurysm/dissecting • Pregnancy complications • Cardiovascular • Marfan syndrome • Treatment outcome • Infant mortality • Gestational age

ABBREVIATIONS

AoD	Aortic dissection
CABG	Coronary artery bypass grafting
CI	Confidence interval
CPB	Cardiopulmonary bypass
CT	Computed tomography
FET	Frozen elephant trunk
GWs	Weeks of gestation
MFS	Marfan syndrome
TAAD	Type A aortic dissection
TAR	Total arch replacement
TBAD	Type B aortic dissection
TEVAR	Thoracic endovascular aortic repair

INTRODUCTION

Despite its rarity, aortic dissection (AoD) associated with pregnancy ranks the third most frequent cause of maternal death due to cardiovascular diseases. Therefore, it is highly relevant for all medical professionals involved in the care of pregnant women, and in particular, those with Marfan syndrome (MFS). In a follow-up study of 31 pregnancies in 19 patients with MFS [1], Kuperstein *et al.* found that pregnant women with MFS, especially those with a dilated aortic root, are at high risk of AoD, even with tight control of blood pressure and heart rate. While a recent meta-analysis revealed that the prevalence of AoD in pregnant women with MFS was 5.3% [2], our previous study showed that MFS was seen in 68% of such patients [3]. However, up to date, clinical experience with AoD in pregnant women with MFS is limited to case reports [4–6] and small cohorts [1, 7–12]. As a result, the optimal management strategy for this clinical catastrophe remains controversial and unestablished [13, 14]. In this study, we seek to report our experience in 30 pregnant women with MFS sustaining AoD over a 21-year period, focusing on treatment strategies and late outcomes.

MATERIALS AND METHODS

Ethics statement

The Ethics Committees of Beijing Anzhen Hospital of Capital Medical University approved submission and publication of this work and waived the need for informed patient consent (No. 2013013X; March 2013).

Patients

Between June 1998 and April 2019, our group has treated 30 women with MFS (by the Ghent or revised Ghent criteria) who developed AoD during pregnancy ($n = 24$, 80%) or postpartum ($n = 6$, 20%). The mean age was 30.7 ± 4.3 years (range 23–40). AoD was type A (TAAD) in 24 (80%) and type B (TBAD) in 6 (20%). According to the 14-day cut-off, acuity was acute in 21 (70%), including 17 TAADs (70.8%) and 4 TBADs (66.7%). Of these, the time from onset to surgery ($n = 17$) or medical treatment ($n = 4$) averaged 3.9 ± 4.0 days (median 2, range 0.2–14). Positive family history was seen in 13 patients (43.3%) and hypertension in 4 (13.3%).

The mean gestational age at the onset of symptoms was 28.3 ± 8.3 weeks of gestation (GWs) (median 31.5 GWs, range 6 GWs to 6 weeks postpartum). AoD occurred in the first, second and third trimesters and the postpartum period in 13.4% (4/30), 33.3% (10/30), 33.3% (10/30) and 20% (6/30). Fourteen TAADs (58.3%) and 2 TBADs (33.3%) occurred in the third trimester or postpartum (Table 1).

All diagnoses were based on symptoms and physical findings and confirmed by transthoracic echocardiography and computed tomographic angiography (CTA) [15]. Before surgery, the mean diameter of the sinuses of Valsalva was 59.6 ± 17.5 mm, which averaged 63.4 ± 17.6 mm and 44.3 ± 3.2 mm in patients with TAAD and TBAD, respectively. The preoperative maximal aortic size was < 45 mm in 12.5% of TAADs (ascending aorta, 3/24) and in 83.3% of TBADs (descending aorta, 5/6), respectively. Moderate-to-severe aortic regurgitation was seen in 23 patients (76.7%), predominantly in patients with type A dissection (22/23). Preoperative malperfusion occurred in 2 patients with TAAD, including stroke and lower limb ischaemia, in one each (3.3%).

Management strategies

Our management strategy (surgical or medical) is based on the type of AoD and gestational age (delivery first or aortic repair first) (Fig. 1). In patients with TAAD, for pregnancies before 28 GWs, urgent surgical repair is recommended with aggressive foetal monitoring or abortion, depending on the extent of AoD and as per the decision of patients and their relatives; for pregnancies after 28 GWs, we would perform urgent caesarean delivery followed by aortic repair, preferably in a single stage. For patients with TBAD, our approach is delivery first, followed by surgical or endovascular repair or medical therapy, unless urgent surgical repair is mandated by malperfusion, visceral ischaemia, persistent pain or impending or contained aortic rupture [3].

Table 1: Baseline patient profile

Variables	Type A dissection (*n* = 24)	Type B dissection (*n* = 6)	Total (*n* = 30)
Age (years), mean ± SD	30.6 ± 4.3	31.0 ± 4.3	30.7 ± 4.3
Acute dissection (<14 days from onset), *n* (%)	17 (70.8)	4 (66.7)	21 (70.0)
Hypertension, *n* (%)	2 (8.3)	2 (33.3)	4 (13.3)
Positive family history, *n* (%)	11 (45.8)	2 (33.3)	13 (43.3)
Diameter of aortic sinuses (mm), mean ± SD	63.4 ± 17.6	44.3 ± 3.2	59.6 ± 17.5
Maximal aortic size (mm), *n* (%)			
<40	0	4 (66.7)	4 (13.3)
40–45	3 (12.5)	1 (16.7)	4 (13.3)
>45	21 (87.5)	1 (16.7)	22 (73.3)
Aortic regurgitation, *n* (%)			
Moderate	6 (25.0)	1 (16.7)	7 (23.3)
Severe	16 (66.7)	0	16 (53.3)
Weeks of gestation at onset, mean ± SD (median)	29.2 ± 8.7 (32)	24.5 ± 8.9 (21.5)	28.3 ± 8.8 (31.5)
Trimester at onset, *n* (%)			
First trimester	2 (8.3)	2 (33.3)	4 (13.3)
Second trimester	8 (33.3)	2 (33.3)	10 (33.3)
Third trimester	9 (37.5)	1 (16.7)	10 (33.3)
Postpartum	5 (20.8)	1 (16.7)	6 (20.0)
Management, *n* (%)			
Medical	1 (4.2)	3 (50.0)	4 (13.3)
Surgical	23 (95.8)	3 (50.0)	26 (86.7)

SD: standard deviation.

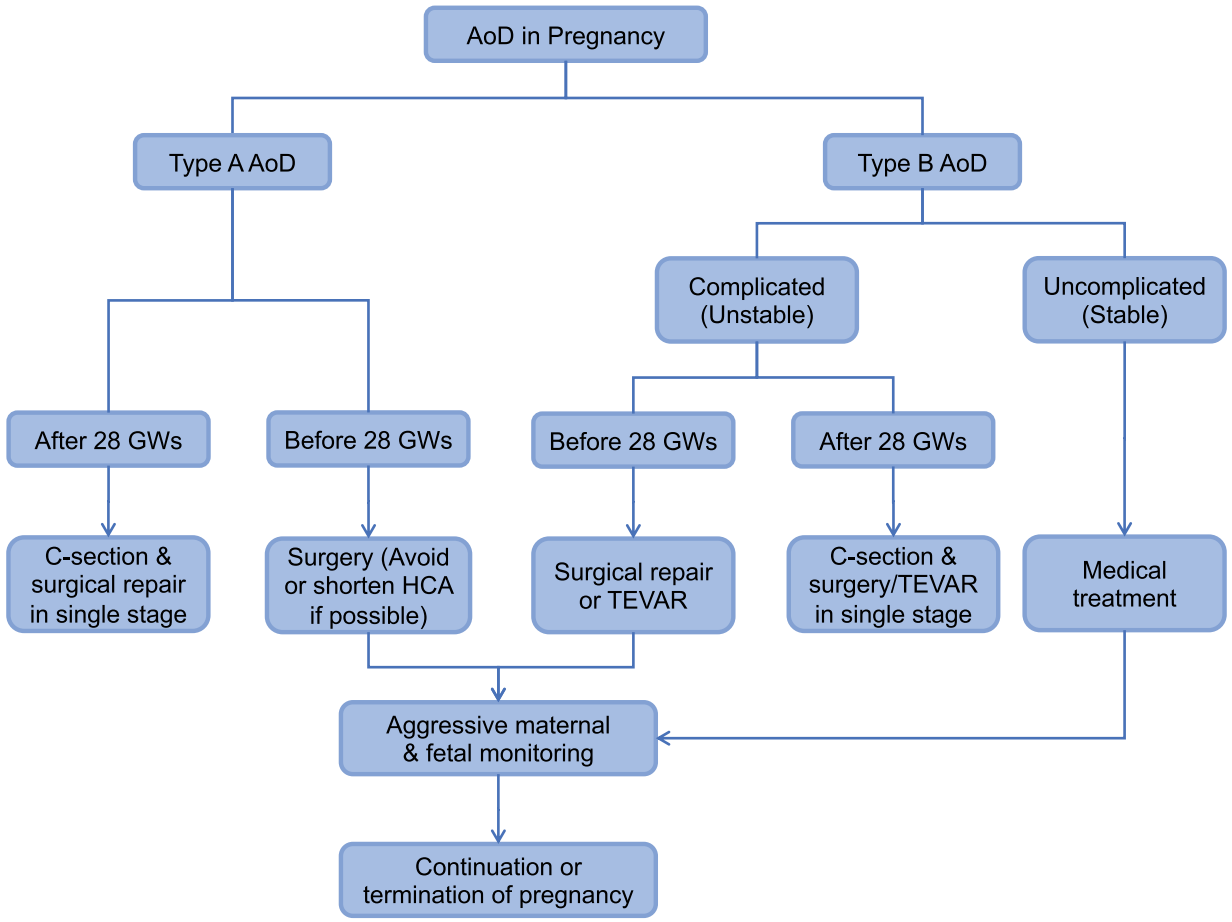


Figure 1: Algorithm for management of aortic dissection in pregnant women with Marfan syndrome. AoD: aortic dissection; GWs: weeks of gestation; HCA: hypothermic circulatory arrest; TEVAR: thoracic endovascular aortic repair.

In this cohort, 26 patients were managed surgically (86.7%) and 4 medically (13.3%). The sequences of aortic repair and delivery were caesarean delivery followed by aortic repair in 2 stages in 12 (41.4%) patients, single-stage delivery followed by aortic repair in 10 (34.5%) patients and aortic repair followed by delivery in 7 (24.1%) patients. After caesarean delivery, a Cook balloon was inserted in the uterus to prevent postoperative bleeding.

Intraoperative management

Surgical repair was performed under cardiopulmonary bypass (CPB) and moderate hypothermia (or normothermia). Our routines of CPB include:

i. Use of histidine-tryptophan-ketoglutarate (HTK) solution for cardioplegia. A single dose of 2000 ml is administered through antegrade infusion, 1200 ml into the left coronary ostia and 800 ml into the right coronary ostia. Removal of the HTK solution is achieved either by suction of the coronary sinus if the right atrium is opened or by ultrafiltration if the right atrium is not opened.
ii. Avoiding circulatory arrest whenever possible.
iii. Minimizing the duration of CPB.
iv. Maintaining high flow rate (>2.4 L/m^2/min) and mean arterial pressure (>70 mmHg).

Our strategies to save a foetus before 28 GWs include:

1. Avoiding use of or shortening hypothermic circulatory arrest (HCA) before 28 GWs whenever possible.
2. Meticulous maintenance of haemostasis (and, in particular, avoiding hypoglycaemia and hypomagnesaemia).
3. Aggressive monitoring of foetal heart and movement.
4. Removing the HTK solution immediately to prevent it from entering systemic circulation.

Patient follow-up

All survivors (mothers and foetuses or neonates) were clinically followed up by clinic visits, letters or phone calls to monitor survival, reoperation and adverse events. Mothers were recommended to have echocardiography and computed tomographic angiography regularly to evaluate the aorta and detect complications. A cross-sectional follow-up for this analysis was made on 25 September 2019.

Statistical analysis

Statistical analysis was performed using SPSS 22.0 for Windows (IBM SPSS, Armonk, NY, USA) and Prism GraphPad for Mac 8.1 (GraphPad Software, San Diego, CA, USA). Data are expressed as mean ± standard deviation (range) or number and percentages as appropriate. Maternal and foetal survival were estimated using the Kaplan–Meier method.

RESULTS

Operative data

Surgical repair was performed in 26 patients, which included composite graft root replacement (Bentall) in 22 (84.6%) patients, ascending aortic replacement in 2 (6.7%) patients, total arch replacement (TAR) in 18 (69.2%) patients, frozen elephant trunk (FET) in 17 (65.4%) patients and descending aortic replacement, thoracoabdominal aortic repair and left carotid–left subclavian bypass in 1 (3.8%) patient each. The details of our FET + TAR technique were described previously [16–18]. Concomitant cardiac procedures included coronary artery bypass grafting (CABG) in 3 (11.5%) patients and mitral valve surgery in 2 (7.7%) patients (Table 2).

Circulatory arrest was used in 19 patients with a mean nasopharyngeal temperature of 23.3 ± 1.6°C (range 19.0–25.1). The times of CPB, aortic cross-clamp and hypothermic circulatory arrest in 17 patients undergoing TAR + FET were 201 ± 44 (range 128–316), 108 ± 24 (range 77–173) and 26 ± 10 (range 12–50) min, respectively. In 6 patients with an isolated Bentall procedure, the nasopharyngeal temperature, CPB and aortic cross-clamp times were 29.7 ± 3.7°C (range 25.2–35.1), 93.8 ± 34.6 (range 50–135) and 62.2 ± 19.2 (range 37–87) min, respectively.

Table 2: Data of surgical procedures

Variables	Type A dissection (n = 23)	Type B dissection (n = 3)	Total (n = 26)
Operative data[a]			
Cardiopulmonary bypass time (min)	185 ± 87 (185)	129.0 ± 53.6 (112)	178 ± 84 (185)
Cross-clamp time (min)	98 ± 32 (99)	70.5 ± 47.4 (70.5)	96 ± 33 (99)
Cerebral perfusion time (min)	26 ± 10 (25)	24.5 ± 11 (24.5)	26 ± 10 (25)
Nasopharyngeal temperature (°C)	25 ± 4 (24.4)	23.5 ± 0.7 (23.5)	25 ± 3.5 (24.1)
Surgical procedures			
Composite graft root replacement	21 (91.3)	1.0 (33.3)	22 (84.6)
Ascending aortic replacement	2 (8.7)	0	2 (7.7)
Total arch replacement + FET	16 (69.6)	1.0 (33.3)	17 (65.4)
Total arch replacement	1 (4.3)	0	1 (3.8)
Descending aortic replacement	1 (4.3)	0	1 (3.8)
Thoraco-abdominal aortic aneurysm repair	0	1.0 (33.3)	1 (3.8)
FET + left carotid–left subclavian bypass	0	1.0 (33.3)	1 (3.8)
Coronary artery bypass grafting	3 (13.0)	0	3 (11.5)
Mitral valve surgery	2 (8.7)	0	2 (7.7)

[a]Data are expressed as mean ± standard deviation (median) or n (%).
FET: frozen elephant trunk; SD: standard deviation.

Type A aortic dissection

Of 24 patients with TAAD, 23 were managed with surgery and 1 elected to have medical treatment. The timing of aortic repair and delivery were delivery first in 7, delivery and surgery in a single stage in 10 and aortic repair first in 6.

Delivery first. Seven patients (30.4%, 7/24) had caesarean delivery first in a different hospital at 35.4 ± 6.1 GWs (median 38; range 22–39) before they were transferred to our institution. Aortic repair was performed after a mean delay of 46 days (range 2–137 days). Ascending aortic replacement + TAR + FET was performed for 1 patient. Six patients underwent Bentall procedure + TAR + FET; among those, 2 had a concomitant mitral valve surgery and 1 had CABG.

Maternal death occurred in 2 (28.3%) patients. The first patient sustained acute renal failure after Bentall + TAR + FET, which necessitated continuous renal replacement therapy. She expired due to multiorgan failure at 20 days. The second patient expired suddenly due to descending aortic rupture at 5 days postoperatively. The foetal mortality was 14.3% (1/7) in this group (Table 3).

Single-stage delivery and aortic repair. In 10 patients (43.5%, 10/23), caesarean section and aortic repair in a single stage was performed at mean 32.0 ± 5.0 GWs (median 33; range 22–38). Surgical procedures included isolated Bentall procedure in 4 patients and Bentall + TAR + FET in 6 patients (one of whom had a CABG for dissection of the right coronary artery).

Maternal and foetal mortalities were 10% (1/10) and 20% (2/10), respectively. Two foetuses (of 33 and 23 GWs) died after caesarean delivery. Acute thrombotic occlusion of the coronary artery graft occurred in a patient following a Bentall + TAR + FET + CABG, which was managed an emergency redo CABG; acute renal failure ensued and she succumbed to multiorgan failure 2 days postoperatively.

Aortic repair first. In 6 patients (26.1%, 6/23), due to the earlier gestational age (before 28 GWs), aortic repair was performed first at 18.0 ± 5.8 GWs on average (median 17.5; range 8–27). Aortic procedures were Bentall + TAR + FET in 3 patients (Fig. 2), isolated Bentall in 2 patients and ascending aortic replacement + TAR + descending aortic replacement + CABG in 1 patient.

Maternal mortality was 16.7% (1/6), which occurred in 1 patient who underwent ascending aortic replacement + TAR + descending aortic replacement + CABG. Descending aortic rupture occurred intraoperatively, which prolonged the CPB time to 6 h. The patient sustained massive cerebral infarct after surgery and expired at 15 days.

After a median delay of 20 days in the intensive care unit (range 1–101, mean 33.2), 5 foetuses were aborted by induced

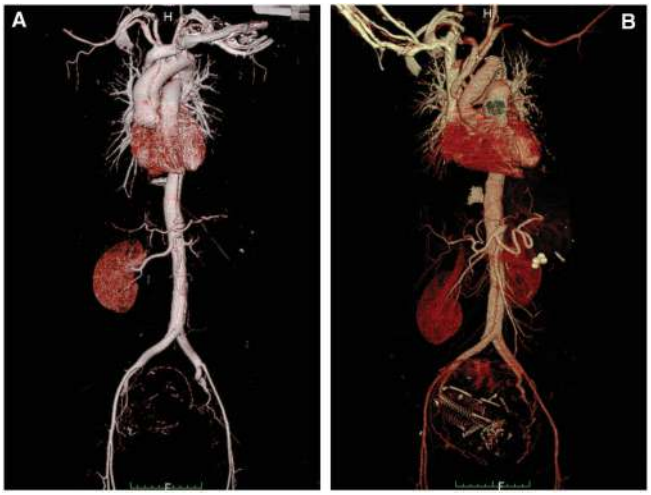


Figure 2: A 26-year-old woman with Marfan syndrome sustained an acute type A dissection at 12 weeks of gestation (**A**). An emergency composite graft root and total arch replacement with frozen elephant trunk followed by aggressive foetal monitoring achieved maternal and foetal survival, as shown by the computed tomography scan at 2 months postoperatively (**B**).

Table 3: Management strategy and outcomes

Variables	Type A dissection ($n = 24$)	Type B dissection ($n = 6$)	Total ($n = 30$)
Timing of aortic repair and delivery, *n* (%)	($n = 23$)	($n = 6$)	($n = 29$)
Delivery followed by aortic repair in 2 stages	7 (30.4)	5 (83.3)	12 (41.4)
Single-stage delivery and aortic repair	10 (43.5)	0	10 (34.5)
Aortic repair before delivery in 2 stages	6 (26.1)	1 (16.7)	7 (24.1)
Early mortality (%),[a] (%) *n*			
Maternal mortality	20.8 (5/24)	16.6 (1/6)	20.0 (6/30)
Delivery first	28.6 (2/7)	20.0 (1/5)	25.0 (3/12)
Delivery and surgery in a single stage	10.0 (1/10)	0	10.0 (1/10)
Aortic repair first	16.7 (1/6)	0	16.7 (1/6)
Medical therapy	100.0 (1/1)	33.3 (1/3)	50.0 (2/4)
Foetal/neonatal mortality	37.5 (9/24)	66.7 (4/6)	43.3 (13/30)
Delivery first	14.3 (1/7)	60.0 (3/5)	33.3 (4/12)
Single-stage delivery and surgery	20.0 (2/10)	0	20.0 (2/10)
Aortic repair first	83.3 (5/6)	100.0 (1/1)	85.7 (6/7)
Medical	100.0 (1/1)	33.3 (1/3)	50.0 (2/4)
Late outcomes	($n = 19$)[a]	($n = 5$)	($n = 24$)
Duration of follow-up (years), mean ± SD	4.1 ± 3.0	2.5 ± 2.4	3.7 ± 2.9
Maternal mortality, *n* (%)	3 (15.8)	1 (20)	4 (16.7)
Estimated maternal survival at 5 years (%)	65.8	37.5	62.1
Foetal/baby survival, (%) *n*	93.3 (14/15)	100 (2/2)	94.1 (16/17)

[a]Early mortality was calculated by the number of expired patients divided by the total number of patients in a group managed with a certain strategy.
SD: standard deviation.

labour at mean 15.8 ± 5.2 GWs (median 14; range 12–23) upon the request of patients and their families. Foetal mortality in this group was 83.3% (5/6). One patient sustaining TAAD at 19 GWs underwent a Bentall procedure at 22 GWs. Fortunately, her foetus survived after surgery and was delivered alive at 38 GWs.

Medical management. One patient with a chronic TBAD developed an acute type A dissection at 25 GWs. Immediate urgent surgery was recommended, but she and her family elected to have medical management first in hope of having single-stage surgical repair and delivery at a later time. Tragically aortic rupture occurred at 8 days from the onset of TAAD despite aggressive anti-impulse therapy, leading to maternal and foetal deaths.

Type B aortic dissection

Of the 6 patients with TBAD, 3 were managed surgically and 3 medically (50% each).

Delivery first. In 5 patients with TBAD, caesarean delivery was performed first at 26 ± 9 GWs (median 22; range 16–37), followed by aortic repair in 2 and medical therapy in 3. Surgical repair included thoraco-abdominal aortic replacement for a dissecting extent II aneurysm after a delay of 90 days, and FET + left carotid–left subclavian bypass for dissected left subclavian artery after 38 days, in 1 patient each.

Maternal and foetal mortalities were 50% (1/2) and 100% (2/2) with surgery and 33.3% (1/3) and 33.3% (1/3) with medical therapy due to aortic rupture, respectively.

Aortic repair first. At 17 GWs, an emergency Bentall procedure + FET + TAR was performed for 1 patient with TBAD and root aneurysm (16.7%, 1/6). After a delay of 2 weeks, a baby was delivered by caesarean section, who unfortunately expired after delivery. The mother survived and was discharged uneventfully.

Maternal and foetal mortality associated with hypothermic circulatory arrest

In 19 patients undergoing hypothermic circulatory arrest, including 17 TAADs and 2 TBADs, maternal mortality was 31.6% (6/19) and foetal mortality was 47.4% (9/19). In 17 type A dissections, the mortality rates were 35.3% for mothers (6/17) and 41.2% for foetuses (7/16). In 2 type B dissections, all mothers survived the operation while foetal mortality was 100% (2/2).

Early foetal survival by gestational weeks

Among 14 pregnancies before 28 GWs and 16 pregnancies after 28 GWs, the early foetal survival before 28 GWs (14.3%, 2/14) was significantly lower compared to that after 28 GWs (93.8%, 15/16; $P < 0.001$).

Late outcomes

Follow-up was complete in 95.8% (23/24) for a mean duration of 3.7 ± 2.9 years (range 0.3–9.8), extending beyond 5 years in 33%. One patient was lost to follow-up.

Late death and reoperation. In the group of TAAD, late deaths occurred in 4 patients (with TAAD in 3 and TBAD in 1) and 2 foetuses/neonates. The first patient with TAAD died of over anticoagulation at 3 months postoperatively after Bentall procedure + TAR + FET + mitral valve replacement. In the second patient computed tomography (CT) scan detected no aortic complications after a composite graft root replacement for a dissecting root aneurysm, but she expired at 4 years due to lymphoma. The third patient with TAAD died of distal aortic rupture at 8 years after Bentall procedure + TAR + FET and her follow-up CT scan showed marked dilation of the thoraco-abdominal aorta. One patient with TBAD expired suddenly at 3 years, which was ascribed to acute retrograde type A dissection by her emergency physician.

Secondary intervention was required in 1 patient with TAAD, who required thoracic endovascular aortic repair (TEVAR) for a new entry tear distal to the FET at 1 month postoperatively.

Late survival. Overall maternal survival was 76.7% at 1 year [95% confidence interval (CI) 57.2–88.1%], 70.7% at 3 years (95% CI 48.8–84.6%) and 64.3% at 6 years (95% CI 40.7–80.5%) (Fig. 3). Survival was 53.1% up to 6 years for children (95% CI 34.0–69.0%) (Fig. 4).

DISCUSSION

While the association between pregnancy and AoD was described as early as in the 1880s [19], it was not until 1944 that Schnitker and Bayer [20] reported the first case of AoD in a pregnant women with MFS (cystic medial necrosis of the aorta) [13, 14]. Because of the rarity and limited clinical experience with AoD in pregnant Marfan women [1, 4–12], it is difficult to formulate conclusive recommendations in current consensus and guidelines on the diagnosis and management of this complex clinical scenario [13, 14]. The specifics and advantages of our work [3, 21] have enabled us to accrue a cohort of 30 such patients over the past 2 decades, which may represent the largest single-team experience and offer valuable insights into the optimal management of AoD in pregnant women with MFS.

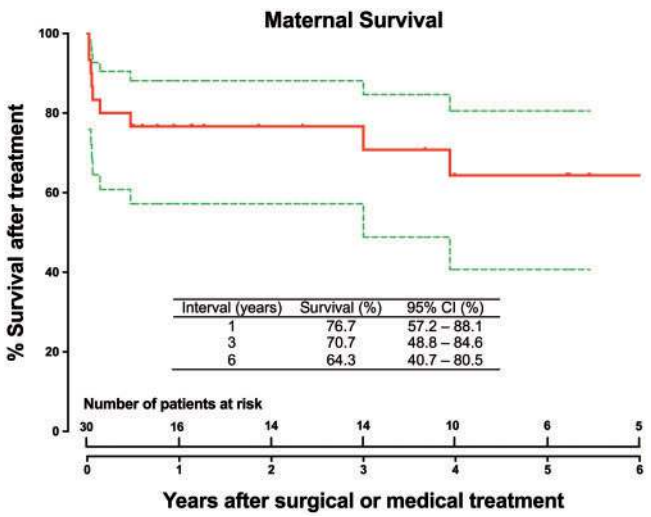


Figure 3: Overall maternal survival after surgical or medical treatment. CI: confidence interval.

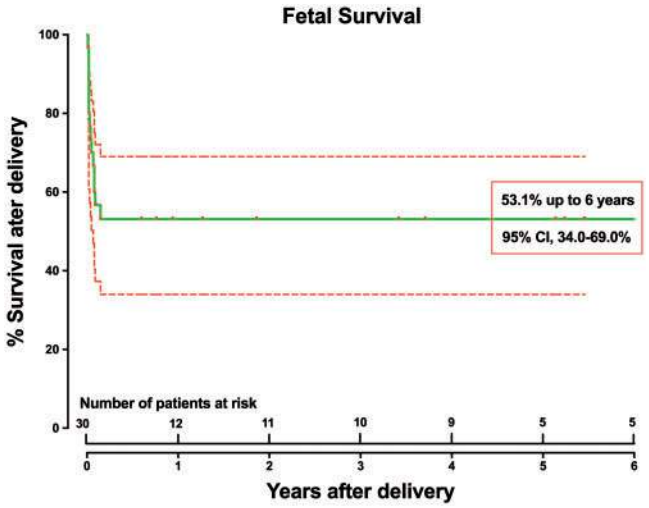


Figure 4: Overall foetal survival after delivery. CI: confidence interval.

The results of this study have proven the validity and efficacy of our management algorithm for pregnancy-related AoD in MFS, which has evolved considerably over time towards the goal of 'saving 2 lives'. Our treatment goal used to be 'saving the mother' during the early years, became 'saving 2 lives and the uterus' with experience accrued and is moving towards 'saving 2 lives before 28 GWs' nowadays.

Recommendations on management algorithm

Based on our experience, we recommend the following algorithm for the management of pregnancy-related AoD in MFS according to the types of dissection and GWs (Fig. 1):

i. For TAAD before 28 GWs, aortic repair should be performed first, followed by aggressive maternal and foetal monitoring, which dictates continuation or termination of pregnancy.
ii. For TAAD after 28 weeks, single-stage delivery and aortic repair is preferred.
iii. For uncomplicated TBAD, medical treatment with aggressive maternal and foetal monitoring is recommended.
iv. For complicated TBAD after 28 weeks, single-stage delivery and surgery or TEVAR is preferred.
v. For complicated TBAD before 28 weeks, surgery or TEVAR is performed first, followed by aggressive maternal and foetal monitoring, which dictates the continuation or termination of pregnancy.

Type A aortic dissection. The results of this study show that a gestational age above 28 weeks significantly improves foetal survival. Therefore, for patients with type A dissection after 28 GWs, it is not difficult to achieve the goal of 'saving 2 lives' using either the 'delivery first' or 'single-stage delivery and aortic repair' strategy. In this cohort, these 2 strategies have achieved a favourable early survival of 82.4% (14/17) for both the mothers and foetuses, respectively.

For patients with TAAD occurring before 28 GWs, saving 2 lives represents a formidable therapeutic challenge with which the multidisciplinary team is confronted [22, 23], even though patients and their relatives often elect to abort the foetuses under such circumstances. According to our experience, management should be tailored to specific pathologies of the aorta. For type A dissections confined to the ascending aorta or the mid-portion of the transverse arch, which does not necessitate distal circulatory arrest during repair, saving the foetus is always a worthwhile and often attainable goal. In this series, among the 6 cases managed with an isolated Bentall procedure, we achieved a maternal survival of 100% and a foetal survival of 66.7% (4/6). For type A dissections involving or extending beyond the distal arch, which entails distal circulatory arrest for aortic repair, the likelihood of foetal survival is low, despite the scattered reports of success in achieving foetal survival in literature [4, 24]. Besides the routine strategies of CPB for cardiac and aortic surgery in pregnancy [25–27], our preferred perfusion approaches in such settings include (i) removing the HTK solution immediately as much as possible to prevent it from entering the systemic circulation and avoid hyperkalaemia and (ii) lowering the nasopharyngeal temperature to 25°C to ensure sufficient blood supply to the brain. Our success in achieving maternal and foetal survival after extended repair, as illustrated by the case in Fig. 2, has proven the efficacy of this perfusion strategy and encouraged us to make further endeavours towards saving 2 lives before 28 GWs.

With respect to the management of the aortic root, although valve sparing root replacement has many advantages and better long-term outcomes in these young patients, in emergency repair for acute dissection and in those with severe aortic regurgitation (16 patients in this series), we prefer composite graft root replacement so as to guarantee the success of the operation and avoid or minimize surgical risks.

Type B aortic dissection. Although it is difficult to make conclusive recommendations based on the small number of patients with TBAD in this series, our preferred approach to type B dissection is a 'delivery first' strategy owing to the suboptimal outcomes with surgical repair. However, aortic repair should be prioritized over delivery for patients with malperfusion and visceral ischaemia, persistent pain and signs of contained or impending aortic rupture. Although TEVAR might be a good option in patients with connective tissue disease [28], in pregnant Marfan women with AoD, we reserve TEVAR as an emergency bailout procedure for those with either acute distal ischaemia (lower limb or viscera) or signs of pending rupture, such as refractory chest or back pain.

The current guidelines of the American Heart Association (AHA) and European Society of Cardiology (ESC) recommend a threshold of 45–50 mm for aortic surgery in patients with MFS [13, 14]. However, 26.7% of pregnant women with MFS in this series (8/30) sustained AoD despite a preoperative maximal aortic size of < 45 mm. Therefore, for women with Marfan syndrome contemplating pregnancy, aortic repair should be considered, even at diameters smaller than recommended by current guidelines.

Limitations

This study is limited by its retrospective nature, small sample size, relatively short duration of follow-up and experience in a single-centre setting, which precludes making conclusive recommendations. Another important weakness pertains to the lack of detailed information on foetal outcomes, such as the neurological outcomes and Apgar score, in all surviving infants, because 12

babies were delivered first in other hospitals before their mothers were transferred. Despite the relatively large number of patients, the level of evidence is limited and our treatment algorithm may not be duplicated in other centres. Further studies in a larger patient population for longer durations, preferably in a multicentre setting are warranted to optimize management strategies and improve outcomes for this rare but complex clinical problem.

CONCLUSIONS

Management of AoD in pregnant women with MFS should be based on the types of AoD (surgical or medical) and gestational age (delivery first or aortic repair first). Maternal and foetal survival are dependent on the GWs and surgical strategies. Given the high mortality *per se*, such patients should be treated at specialized multidisciplinary centres. Aortic repair should be considered prior to pregnancy in women with Marfan syndrome, even at smaller aortic diameters than recommended by current guidelines.

Funding

This work was supported by Beijing Major Science and Technology Projects from the Beijing Municipal Science and Technology Commission [Z171100001017083 & Z19110700660000] and the National Science and Technology Support Program [2015BAI12B03].

Conflict of interest: none declared.

Author contributions

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