Usefulness of Stenting in Aortic Coarctation in Patients With the Turner Syndrome

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We report our experience with stent implantation for treatment of aortic coarctation in patients with Turner syndrome. Ten consecutive patients with Turner syndrome and aortic coarctation (median age 12 years, range 9 to 24) underwent coarctation stenting. Of these, 6 patients were treated for isolated coarctation and 4 for recurrent coarctation (3 after balloon dilation and 1 after balloon dilation and surgical repair). Bare metal stents were implanted in 7 patients and covered stents in 3. Immediately after stent implantation, peak systolic gradient decreased from 46.1 ± 24.3 to 1.9 ± 2.1 mm Hg ($p < 0.001$). Aortic diameter at coarctation site increased from 5.1 ± 3.2 to 15.3 ± 2.0 mm after stenting ($p < 0.001$). There were no deaths or procedure-related complications. During a median follow-up of 30.5 months, no patient developed restenosis. Two patients developed late aortic aneurysms at the coarctation site. In conclusion, stent implantation for aortic coarctation in patients with Turner syndrome appears to be a safe and effective alternative to surgical repair. Larger cohorts and longer-term follow-up are required to determine the effects of the procedure on the aortic wall. **(Am J Cardiol 2010;106:1327–1331)**

General treatment options for coarctation of the aorta (COA) are surgery, balloon angioplasty, and stenting. Selection of the optimal therapy for COA in Turner syndrome is difficult due to the paucity of information about the safety of treatment options in this population. Aortic wall abnormalities in Turner syndrome including cystic medial necrosis and reports on higher mortality and morbidity after surgical repair, a fatal stent redilation report, and small number of reported COA stenting procedures in these patients make selection of the optimal treatment method difficult.[1–3] We report on 10 patients with Turner syndrome and stented COA, which is, to the best of our knowledge, the largest cohort reported thus far. We also present a review on existing evidence about the safety of each therapeutic option, focusing on aortic wall injuries and mortality.

Methods

Patients were enrolled in the study from March 1997 to December 2009 from 7 congenital heart disease centers. They were collected by an e-mail announcement from the Congenital Cardiovascular Interventional Study Consortium mailing list. Inclusion criteria were the presence of COA, pure or mosaic 45,XO karyotype, and weight >30 kg for safe stent implantation. The study excluded patients with hypoplastic distal aortic arch and/or aortic isthmus and those with complex CoA, defined as complete near atresia and associated aneurysm. Hypoplasia was defined as a ratio of the aortic arch or isthmus diameter to the descending aorta diameter at the level of the diaphragm <0.6. After obtaining informed consent from the patient or guardians, COA stenting was done as described in other reports.[4] Implanted were 3 Palmaz 4014 stents (Johnson and Johnson Intervention Systems, Warren, New Jersey), 3 covered Cheatam Platinum stents (NuMED, Hopkinton, New York), 2 Palmaz-Genesis XD stents (Cordis Europa, Roden, Netherlands), and 2 bare Cheatam Platinum stents. For stent dilation 3 Balloon in Balloon (NuMED), 3 Cristal (BALT, Montmorency, France), 2 PEMT (Meditech, Watertown, Massachusetts), 1 SciMed (Boston Scientific-Scimed, Minneapolis, Minnesota), and 1 Z-med II (NuMED) balloon catheters were used. Imaging methods used during follow-up were computed tomography (8 patients), magnetic resonance imaging (4 patients), and angiography (2 patients).

We searched MEDLINE through PubMed and Google search engines using a combination of the terms "coarctation" and "Turner." Inclusion criteria were report of COA treatment in patients with Turner syndrome by any of the 3 methods (surgery, balloon angioplasty, and stenting) and longer than immediate follow-up data on aortic wall injuries and mortality. We excluded reports of extra-anatomic repair because it is a different treatment strategy and is rarely indicated in patients with COA.

Descriptive statistics such as mean ± SD, median, and frequency were calculated for each demographic and clinical characteristic whenever appropriate. Paired-sample *t* tests were used to compare pressure gradients and aortic

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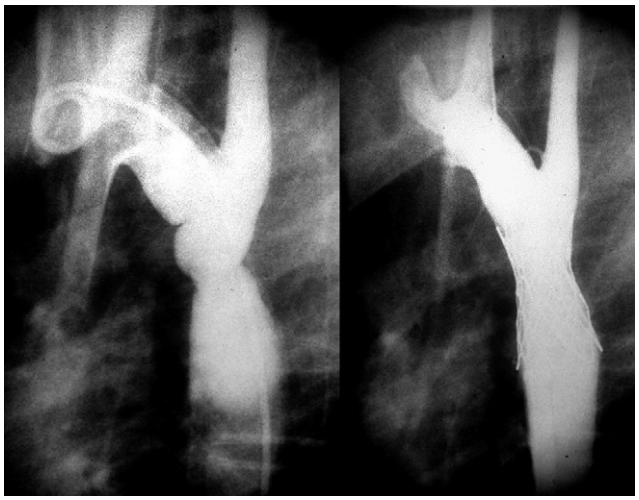

Figure 1. Aortograms of patient 8 before *(left)* and after *(right)* stenting with a covered Cheatam Platinum stent.

diameters. A 2-sided p value <0.05 was considered indicative of statistical significance.

Results

We included 10 consecutive patients with Turner syndrome in the study cohort. Overall, 7 patients had 45,XO karyotype and 3 had mosaic 45,XO/46,XX karyotype. Median age was 12.1 years (range 9.1 to 23.7), and weight and height were 40 kg (range 31 to 55) and 139 cm (range 130 to 157), respectively. All coarctations were discrete in type (Figure 1). Four patients had a history of COA balloon angioplasty and 1 of them had a history of COA surgical repair. With respect to cardiac co-morbidities, 3 patients had a bicuspid aortic valve, 1 of whom had severe aortic stenosis. Other co-morbidities included hypothyroidism in 2 patients, with horseshoe kidney, thrombocytopenia, and scoliosis in each patient. Baseline demographics, peak gradients before and after stenting, and methods of follow-up are presented in Table 1.

Peak transcoarctation gradient before stenting was 46.1 ± 24.3 mm Hg, which was decreased to 1.9 ± 2.1 mm Hg after stenting ($p <0.001$). Aortic diameter at coarctation site increased from 5.1 ± 3.2 to 15.3 ± 2.0 mm after stenting ($p <0.001$). No immediate deaths or periprocedural complications occurred.

Patient 7 had also a bicuspid valve with severe aortic stenosis (peak pressure gradient 93 mm Hg). Balloon valvuloplasty was not feasible because the catheter could not pass through the calcified aortic valve. A decision was made to stent the COA and repair the aortic valve surgically. The patient developed chest pain after stenting, which was relieved by antianginal medication and disappeared 2 days later. Twelve-lead electrocardiogram, cardiac enzymes, and computed tomogram were normal. Whether the pain resulted from decreased coronary perfusion pressure or a small tear in the aortic wall cannot be confirmed. The patient underwent successful elective surgical valvotomy 2 months after stenting (peak pressure gradient 33 mm Hg and trivial aortic regurgitation postoperatively).

Median follow-up period was 30.5 months (range 33 days to 10 years). No death occurred during that period. During the follow-up period, small aneurysms were detected in 2 patients (20%). One of the aneurysms occurred distal to the stented area and was first detected by computed tomography 8 months after stenting (patient 7; Figure 2). The other was also detected by spiral computed tomography in the middle portion of a bare stent 1 month after stenting (patient 6; Figure 2).

After a median interval of 41.3 months, 2 stents were redilated (patients 1 and 2). Peak transcoarctation gradient before redilation was 11.0 ± 1.4 mm Hg, which decreased to 0 thereafter. Neither redilation led to death or any major complication.

Results of the literature review are presented in Table 2. In total, 46 surgical procedures, 49 cases of balloon angioplasty, and 15 stent implantations have been reported in patients with Turner syndrome. With respect to morbidity and mortality, balloon angioplasty was the safest reported procedure (2% and 0%, respectively), followed by stenting (20% and 6.6%) and surgery (30% and 11%).

Discussion

We demonstrated that COA stenting is a safe and effective procedure at midterm follow-up in a small cohort of patients with Turner syndrome. Taking into account the cases reported thus far, it appears that stenting is not inferior to the other treatment methods with regard to morbidity and mortality.

Surgical repair of COA is still the standard method of care to which novel methods are compared and remains the only option when endovascular therapies fail or become complicated. Morbidity of surgical repair is 11%, considerably lower than balloon angioplasty (19%) but higher than stenting (9%).[5] Although until recently no cases of aortic aneurysms after surgical repair have been reported,[5] Qureshi et al[6] reported that 10% of patients with previous COA surgery had evidence of aneurysm formation. Reports on surgical repair of COA in patients with Turner syndrome have demonstrated that mortality and risk of aortic wall injury were highest among the 3 treatment strategies (Table 2). Aortic wall injuries (dissection, aneurysm formation) and their consequences (hemorrhage) occurred in 1/3 of reported operations. Operative mortality was 11%, which is higher than in genetically normal subjects. Ravelo et al[3] reported 1 death in 8 patients with Turner syndrome versus only 1 in 345 coarctation repairs in patients without Turner syndrome.

Potential problems of balloon angioplasty including restenosis, aneurysm formation, and procedural failure have generated a controversy on its use. Formation of aortic aneurysms has been reported in 0% to 45% of patients who had undergone balloon angioplasty.[6,7] With regard to mortality, no statistical difference was found between patients who had undergone percutaneous balloon aortoplasty (1 of 30) versus patients with a surgical repair (2 of 28).[8] Reported COA balloon angioplasties in patients with Turner syndrome carried the lowest risks of aortic wall injury (2%) and mortality (0%) among the 3 options. However, these rates seem to be underestimated because they are lower than

Table 1
Demographic, clinical and echocardiographic characteristics of the study population at baseline and after follow-up

Patient	Age (years)	Karyotype	Previous Procedures	PG Before Stenting (mm Hg)	PG After Stenting (mm Hg)	Method of Follow-Up		
						Angiography	CT	MRI
1	9.1	Mosaic	BA	40	0	+	+	+
2	10.2	XO	BA	30	5	+	0	+
3	11.1	XO	Surgery, BA	50	2	0	+	+
4	12.0	Mosaic	0	80	5	0	+	0
5	12.1	XO	BA	32	2	0	0	+
6	12.2	XO	0	90	0	0	+	0
7	13.0	Mosaic	0	30	0	0	+	0
8	16.9	XO	0	33	1	0	+	0
9	18.5	XO	0	14	0	0	+	0
10	23.7	XO	0	62	4	0	+	0

BA = balloon angioplasty; CT = computed tomography; MRI = magnetic resonance imaging; PG = peak gradient.

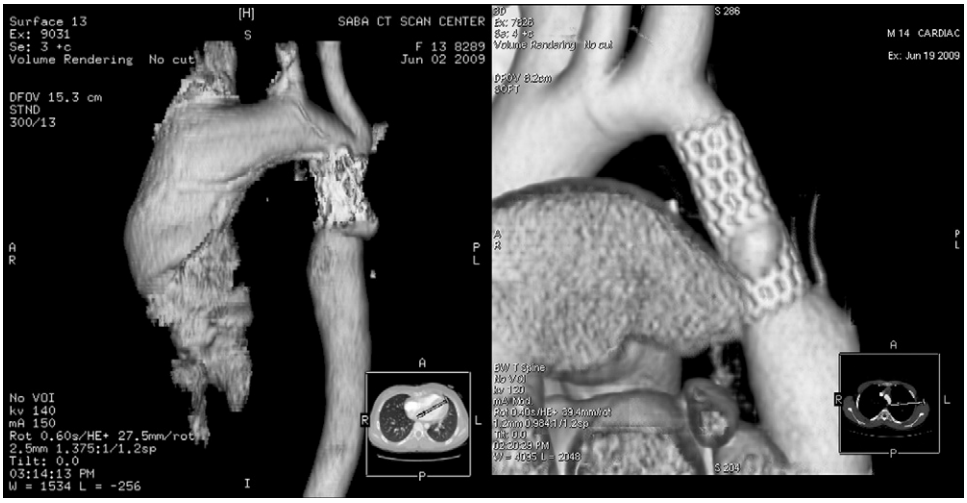

Figure 2. Computed tomographic scans of patients 7 *(left)* and 6 *(right)* in whom small aortic aneurysms developed. *(Left)* Aneurysm distal to a covered Cheatam Platinum stent. *(Right)* Aneurysm in area stented by a Palmaz Genesis XD stent.

those in the general COA population. This may be due to the limitation that many patients were followed only by echocardiography and chest x-ray.[9] Rao et al[10] studied 3 patients with aortic aneurysm after balloon angioplasty but they did not distinguish their 2 patients with Turner syndrome from the others. A recent survey from 16 institutions reported 31 balloon angioplasties but ≥1 of them was part of COA stenting and method of follow-up was not analyzed in detail.[11] In addition, follow-up duration was not mentioned in some reports and when included it was relatively short; the longest was 3 years.[9]

Stenting is the most recently available treatment option, accepted by many experts as the first choice for adult patients and it can be safely applicable in children.[12] However, risk of aneurysm formation after stenting appears to be significant and rates range from 6% (median follow-up 2.8 years) to 12 % (median follow-up 1 year).[13] Forbes et al[14] reported a 3.9% incidence of immediate aortic wall injury after COA stenting in 565 procedures, whereas Qureshi et al[6] found acute aortic wall injury in 2% of a cohort of 153 patients with COA. Aortic rupture may be a rare but fatal complication of stenting but mortality of the procedure is generally low.[15] Stenting of COA is the least practiced method in Turner syndrome, perhaps due to a reported case of staged stent dilation in such a patient, which developed a fatal dissection after redilation.[2] The patient's mother had previously died from aortic dissection. Pathologic examination of the mother's aortic tissue and genetic study demonstrated findings similar to those seen in patients with Marfan syndrome. Thus, presence of Turner syndrome per se might not be the only genetic abnormality predisposing to dissection in that patient. Overall, aortic wall injury and mortality rates were 20% and 6.6%, respectively, after COA stenting in patients with Turner syndrome. These are clearly higher than those in genetically normal subjects,[6,13–15] but intermediate among the 3 options in patients with Turner syndrome. In contrast to the reported cases of balloon angioplasty, all patients with stenting patients were followed-up by ≥1 of the more accurate imaging techniques (computed tomography, magnetic resonance imaging, and angiography).[2,4,9] Use of covered stents may be advisable in patients with Turner syndrome because these can cover the injured wall in the stented area. Avoidance of staged stent redilation has been previously suggested because none of the 15 initial dilations reported thus far caused a major complication, whereas 1 of the 3 redilations was fatal.[2]

Table 2
Complications and mortality of the three available treatment options in patients with Turner syndrome and aortic coarctation

Treatment Option	Reference	Year	Procedures	Complications	Deaths
Surgery	Wray et al[16]	1975	1	Dissection	1
	Ravelo et al[3]	1980	8	3 aortic ruptures	1
	Brandt et al[1]	1984	11	2 bleedings	1
	Lin et al[17]	1986	1	Dissection	—
	Martin et al[18]	1988	1	Aneurysmal dilatation	—
	Ota et al[19]	1992	2	1 aortic tear, 1 aneurysm	1
	Imamura et al[20]	1995	1	—	—
	Kusaba et al[21]	1995	1	—	—
	Sybert et al[22]	1998	1	Aortic ballooning	—
	Counil et al[23]	1999	1	—	—
	Douchin et al[24]	2000	2	—	—
	Badmanaban et al[25]	2003	1	Dissection	—
	Ho et al[26]	2004	4	—	—
	Korpal-Szczyrska et al[27]	2005	9	1 aortic wall injury	1
	Belov et al[28]	2007	1	Dissection	—
	Present report		1	0	0
	Total	—	46	14 (30.4%)	5 (10.8%)
Balloon angioplasty	Mendelsohn e al[29]	1994	7	No aneurysm	—
	Imamura et al[20]	1995	1	—	—
	Rao et al[10]	1996	2	?*	—
	Park et al[30]	2000	2	—	—
	Korpal-Szczyrska et al[27]	2005	2	—	—
	Kataoka et al[9]	2006	1	—	—
	Silberbach[11]	2006	30*	1 aneurysm	—
	Present report		4	—	—
	Total	—	49	1 (2%)	0
Stenting	Thanopoulos et al[4]	2000	2	—	—
	Fejzic and van Oort[2]	2005	1	Dissection at redilation	1
	Kataoka et al[9]	2006	2	—	—
	Present report		10	2 small aneurysms	—
	Total		15	3 (20%)	1 (6.6%)

* See text.

Several factors may have influenced the present results of the 3 treatment procedures in patients with Turner syndrome. These include bias in case reports, unreported procedures, and undiagnosed Turner syndrome in patients with COA. Moreover, different stents were used; therefore, it is not clear whether complications were due to use of the older stent models, method of implantation, or Turner syndrome itself. In general, it is difficult to compare the results of the present study to those published in the literature because patient mix is heterogenous in age, indication of treatment, and coarctation anatomy. However, these data may be helpful until a randomized clinical trial can shed light on the relative safety of each therapeutic option for COA in patients with Turner syndrome.

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