Surgical Repair of Supravalvular Aortic Stenosis in Children With Williams Syndrome: A 30-Year Experience

Tyson A. Fricke, MBBS, BMedSci, Yves d'Udekem, MD, PhD, Christian P. Brizard, MD, Gavin Wheaton, MBBS, Robert G. Weintraub, MBBS, and Igor E. Konstantinov, MD, PhD

Departments of Cardiac Surgery and Cardiology, Royal Children's Hospital, the University of Melbourne, and Murdoch Children's Research Institute, Melbourne, Victoria; and Women's and Children's Hospital, Adelaide, South Australia, Australia

Background. **Williams syndrome is an uncommon genetic disorder associated with supravalvular aortic stenosis (SVAS) in childhood. We reviewed outcomes of children with Williams syndrome who underwent repair of SVAS during a 30-year period at a single institution.**

Methods. **Between 1982 and 2012, 28 patients with Williams syndrome were operated on for SVAS. Mean age at operation was 5.2 years (range, 3 months to 13 years), and mean weight at operation was 18.6 kg (range, 4.1 to 72.4 kg). Associated cardiac lesions in 11 patients (39.3%) were repaired at the time of the SVAS repair. The most common associated cardiac lesion was main pulmonary artery stenosis (8 of 28 [28%]).**

Results. **A 3-patch repair was performed in 10 patients, a Doty repair in 17, and a McGoon repair in 1 (3.6%). There were no early deaths. Follow-up was 96% complete (27 of 28). Overall mean follow-up was 11.2 years (range, 1 month to 27.3 years). Mean follow-up was 5 years (range, 1 month to 14.3 years) for the 3-patch repair patients and 14.7 years (range, 6 weeks to 27 years) for the Doty repair patients. Of the 17 Doty patients, there were 4 (24%) late deaths, occurring at 6 weeks, 3.5 years, 4 years, and 16 years after the initial operation. There were no late deaths in the 3-patch repair patients. Overall survival was 86% at 5, 10, and 15 years after repair. Survival was 82% at 5, 10 and 15 years for the Doty repair patients. Overall, 6 of 27 patients (22%) patients required late reoperation at a mean of 11.2 years (range, 3.6 to 23 years). No 3-patch repair patients required reoperation. Overall freedom from reoperation was 91% at 5 years and 73% at 10 and 15 years. Freedom from reoperation for the Doty repair patients was 93% at 5 years and 71% at 10 and 15 years.**

Conclusions. **Surgical repair of SVAS in children Williams syndrome has excellent early results. However, significant late mortality and morbidity warrants close follow-up.**

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Williams syndrome is a rare congenital disorder associated with cardiac defects in children, most commonly supravalvular aortic stenosis (SVAS). SVAS occurs in approximately 45% to 70% of children with Williams syndrome and requires a surgical repair in approximately 1 in 3 or 4 [1, 2]. Several surgical techniques exist for the repair of SVAS. In 1961, McGoon and colleagues [3] described the single-patch repair of the noncoronary sinus. Later, Doty and colleagues [4] introduced a pantaloon patch repair of the noncoronary and right coronary sinuses. Subsequently, Brom [5] described a 3-patch repair of all 3 aortic sinuses. Other authors have published their experience with slide aortoplasty [6, 7]. We previously described our current technique of a 3-patch repair with extension of the noncoronary sinus patch into the ascending aorta [8].

Patients operated on for SVAS represent a heterogeneous group, because SVAS is also seen in patients with familial elastin arteriopathy and in sporadic cases [9]. Previous studies of SVAS outcomes have included all patients with SVAS and have not specifically looked at patients with Williams syndrome. Williams syndrome patients have comprised between 14% and 60% of patients in these studies [10–13] (Table 1). Thus, few data exist specifically on the outcomes of repair of SVAS in children with Williams syndrome. In this study we sought to determine outcomes of 28 patients with Williams syndrome who underwent surgical repair for SVAS during a 30-year period at a single institution.

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Address correspondence to Dr Konstantinov, Royal Children's Hospital, Flemington Rd, Parkville, VIC 6009, Australia; e-mail: igor.konstantinov@rch.org.au.

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Abbreviations and Acronyms

AVR = aortic valve replacement
CABG = coronary artery bypass graft
LAD = left anterior descending artery
LITA = left internal thoracic artery
LVAD = left ventricular assist device
MPA = main pulmonary artery
MV = mitral valve
PA = pulmonary artery
SVAS = supravalvular aortic stenosis

Material and Methods

This retrospective study was approved by the Royal Children's Hospital Human Research Ethics Committee.

Patients

Between April 1982 and March 2012, 28 patients with Williams syndrome underwent operations for SVAS at the Royal Children's Hospital; of these, 3-patch repair was performed in 10 patients, a Doty repair in 17 , and a McGoon repair in 1. Nine of the last 10 SVAS repairs were 3-patch repairs (Table 2). Table 3 summarizes the preoperative data. Eighteen patients (64%) were boys and 10 (36%) were girls. Mean age at operation was 5.2 years (range, 3 months to 13 years), and mean weight at operation was 18.6 kg (range, 4.1 to 72.4 kg). The SVAS was localized in 24 patients (86%) and was diffuse in 4 (16%). The 4 patients with diffuse disease had involvement of the aortic arch. In 3 of them the aortic arch was patched, including 1 patient who had concomitant patching extending into the left common carotid artery, and an end-to-side coarctation repair was performed in 1 patient. One patient (3.6%) was operated on before the SVAS repair. This patient underwent pericardial patch repair of the main pulmonary artery (MPA) and right pulmonary artery, infundibulectomy, and transannular patching at age 4 months age before undergoing a 3-patch repair at age 5 years.

Associated cardiac lesions in 11 patients (39.3%) were repaired at the time of the SVAS repair. The most common associated cardiac lesion was MPA stenosis (28%). Eleven patients (39.3%) had concomitant procedures with the SVAS repair. The most common concomitant procedure was pericardial patch repair of MPA stenosis (17.9% [5 of 28]). The mean preoperative peak gradient was 71 mm Hg (range, 30 to 144 mm Hg).

Table 1. Number of Williams Syndrome Patients in Supravalvular Aortic Stenosis Outcome Studies

Study First Author	Study Period	SVAS Repair Patients No.	Williams Syndrome Patients No. (%)
Brown [10]	1962–2000	101	14 (14)
Hickey [11]	1976–2006	47	28 (60)
Kaushal [12]	1990–2008	20	10 (50)
Metton [13]	1995–2007	34	14 (41)

SVAS = supravalvular aortic stenosis.

Definitions

Early death or reoperation was defined as death or reoperation occurring before hospital discharge or within 30 days of the operation. Late death or reoperation was defined as death or reoperation occurring after discharge and more than 30 days after the operation.

Surgical Technique

SVAS was repaired using one of three techniques (Fig 1 and Fig 2). Standard techniques were used to establish cardiopulmonary bypass. A Doty repair in 17 patients was performed using an inverted Y-shaped incision into the noncoronary and right coronary sinuses and insertion of a pantaloon patch. An extended 3-patch repair with extension of the noncoronary sinus patch [8] was used in 10 patients. A McGoon repair with a single incision into the noncoronary sinus and insertion of a single patch was used in 1 patient.

Statistical Analysis

Data were imported into Stata 10 software (StataCorp LP, College Station, TX). Continuous variables are reported as a mean with an accompanying range. Kaplan-Meier curves were constructed to display freedom from the study's outcomes.

Results

Early Deaths

There were no early deaths. Table 4 summarizes the intraoperative data. There was 1 (4%) early reoperation. This patient underwent a McGoon repair with mitral valve repair for a prolapsed anterior leaflet at age 6 months and underwent a redo mitral valve repair 16 days later.

Late Outcomes

Follow-up was 96% complete (27 of 28). Overall mean follow-up was 11.2 years (range, 1 month to 27.3 years).

Table 2. Type of Supravalvular Aortic Stenosis Repairs by Era

Era	SVAS Repairs	3-Patch Repairs	Doty Repairs	McGoon Repairs
1982–1992	12	0	12 (7 Dacron,[a] 1 GoreTex,[b] 1 Tascon,[c] 1 homograft)	0
1992–2002	9	4 (1 GoreTex)	5 (2 homograft)	0
2002–2012	7	6	0	1
1982–2012	28	10	17	1

[a] DuPont, Wilmington, Delaware. [b] W.L. Gore and Associates, Flagstaff, Arizona. [c] Tascon Medical Technology Corporation, Los Angeles, California.

SVAS = supravalvular aortic stenosis.

Table 3. Preoperative Data

Variables[a]	Overall (n = 28)	3-Patch Repair (n =10)	Doty Repair (n = 17)	McGoon Repair (n = 1)
Age at operation, years	5.2 (0.3–13.1)	5.2 (3.4–11.1)	5.1 (0.3–13.1)	0.6
Weight at operation, kg	18.6 (4.1–72.4)	18.6 (9.6–38)	18.0 (4.1–72.4)	6.3
Supravalvular aortic stenosis				
Localized	24	9	14	1
Diffuse	4	1	3	0
Associated anomalies	12	2	9	1
Main PA stenosis	8	1	6	1
Branch PA stenosis	5	1	4	0
Hypoplastic aortic arch	3	0	3	0
Coarctation of aorta	1	1	0	0
Left common carotid artery stenosis	2	0	2	0
Bicuspid aortic valve	1	0	1	0
Severe mitral regurgitation	1	0	0	1

[a] Continuous data are presented as mean (range) and categoric data as number of patients.

PA = pulmonary artery.

Mean follow-up was 5 years (range, 1 month to 14.3 years) for the 3-patch repair patients, 14.7 years (range, 6 weeks to 27 years) for the Doty repair patients, and 9.3 years for the patient who had a McGoon repair. The mean postoperative echocardiographic peak gradient was 19 mm Hg (range, 4 to 78 mm Hg), and no patient had more than mild aortic valve regurgitation at the last follow-up.

LATE SURVIVAL. There were 4 late deaths (24%) in the 17 the Doty repair patients, occurring at 6 weeks, 3.5 years, 4 years, and 16 years after the initial operation.

Patient 1 underwent a 3-patch repair and patching of MPA stenosis at age 3 months and died 6 weeks after the operation. The patient was readmitted for seizures before having a cardiac arrest on the ward. The patient had a further cardiac arrest while undergoing cardiac catheterization and died 12 hours later with a refractory metabolic acidosis and low cardiac output syndrome.

Patient 2 had a 2-patch repair at age 4 years and aortic valve replacement with a 19-mm St. Jude mechanical prosthesis (St. Jude Medical, St. Paul, MN) and a Konno procedure at age 11 years, with a permanent pacemaker inserted 10 days later for complete heart block. At age 20 years, this patient had a Bentall-Konno procedure with a 27-mm St. Jude prosthesis with a 27-mm Hemashield graft (Boston Scientific Corp, Natick, Mass) and mitral valve repair. The patient had a cardiac arrest in the immediate postoperative period and was placed on extracorporeal membrane oxygenation. The extracorporeal membrane oxygenation support was discontinued on day 2 postoperatively due to brain death.

Patient 3 died unexpectedly 4 years after operation. The cause of death was unknown.

Patient 4 underwent SVAS repair and patching of MPA stenosis at age 18 months and underwent patch enlargement of the innominate artery and aortic arch for severe systemic hypertension at age 5 years. The patient could not be weaned off of left ventricular assist device support after several days, and a decision was made to withdraw treatment.

No late deaths occurred in the 3-patch repair patients. Overall survival was 86% at 5, 10, and 15 years after repair. Survival was 82% at 5, 10, and 15 years for the Doty repair patients (Fig 3).

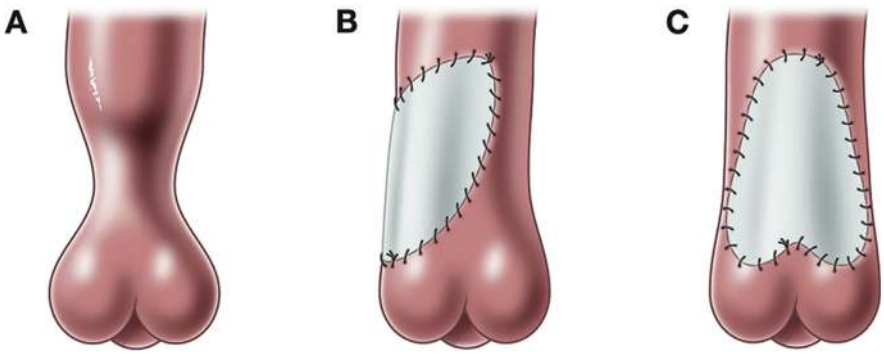

Fig 1. One-patch repair of supravalvular aortic stenosis. (A) Supravalvular aortic stenosis.(B) McGoon repair. (C) Doty repair.

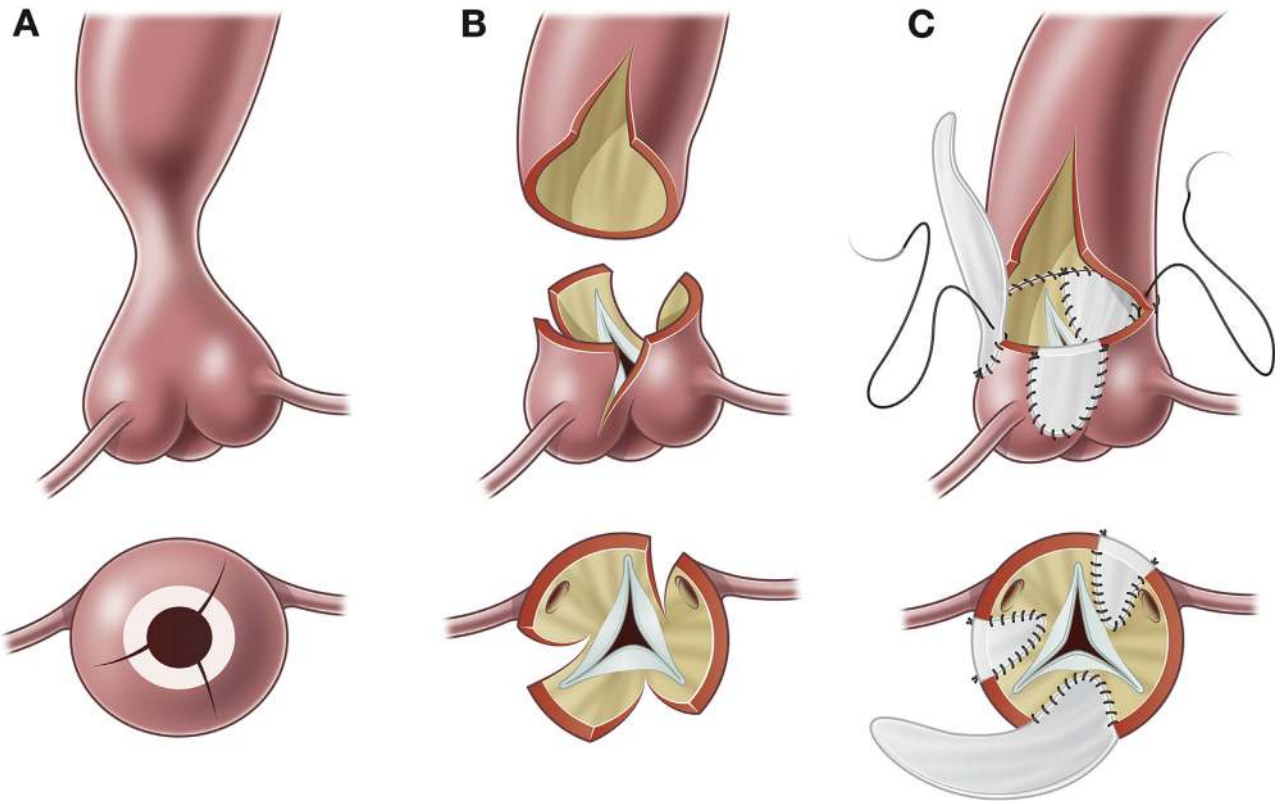

Fig 2. Extended 3-patch supravalvular aortic stenosis repair. (A and B) The ascending aorta is transected at its narrowest point, and 3 incisions are extended into the sinuses of Valsalva. (C) The sinuses are enlarged with 3 pericardial patches, and the patch from the noncoronary sinus is extended into the ascending aorta to ensure symmetrical enlargement of the narrow segment.

LATE REOPERATION. Overall, 6 of 27 patients (22%) required late reoperation at a mean of 11.2 years (range, 3.6 to 23 years) after their operation. Late reoperations were performed in 5 of the 17 Doty patients (29%) and in the McGoon repair patient. No 3-patch repair patients underwent reoperations. Overall freedom from reoperation was 91% at 5 years and 73% at 10 and 15 years. Freedom from reoperation for the Doty repair patients was 93% at 5 years and 71% at 10 and 15 years (Fig 4).

Table 5 lists the reoperations performed. Reoperation was for progression of disease of the aorta or aortic arch in 5 patients and for complex left ventricular outflow

Table 4. Intraoperative Data

Variables[a]	Overall (n = 28)	3-Patch Repair (n = 10)	Doty Repair (n = 17)	McGoon Repair (n = 1)
Associated repair	11	1	9	1
Main PA repair	6	0	6	0
Branch PA repair	4	0	4	0
Arch repair	3	0	3	0
Left common carotid artery stenosis repair	2	0	2	0
Coarctation repair	1	1	0	0
Mitral valve repair	1	0	0	1
Aortic valve repair	0	0	0	0
Cardiopulmonary bypass time, min	116 (57–347)	116 (89–201)	114 (57–227)	347
Aortic cross-clamp time, min	69 (27–180)	92 (68–127)	65 (27–149)	180
Circulatory arrest used	3	1	2	0
LVAD used	2	0	1	1

[a] Continuous data are presented as mean (range) and categoric data as number of patients.

LVAD = left ventricular assist device; PA = pulmonary artery.

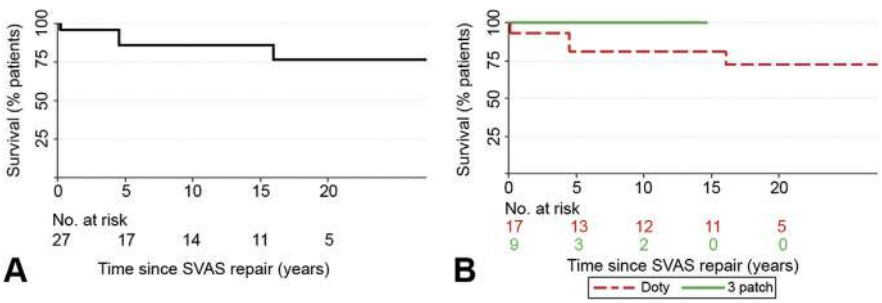

Fig 3. Kaplan-Meier (A) overall survival of children after supravalvular aortic stenosis (SVAS) repair and (B) survival after Doty (red) and 3-patch repair (green).

tract obstruction in 1 patient. One of the 27 patients (4%) required reoperation for restenosis at the site of initial repair. One patient (4%) had an out of hospital fibrillatory cardiac arrest, and a coronary angiogram demonstrated left main coronary artery stenosis. The patient underwent coronary artery bypass with left internal thoracic artery anastomosis to left anterior descending coronary artery.

Comment

SVAS is a rare lesion with few data on outcomes after repair, especially in patients with Williams syndrome. Our results show excellent early outcomes in 28 children with Williams syndrome who underwent surgical repair of SVAS. Favorable early results have previously been demonstrated after SVAS surgical repair for Doty and 3-patch repairs. Bakhtiary and colleagues [14] retrospectively reviewed a cohort of 21 children who had a Doty repair, with Williams syndrome present in 14 of these patients. There were no deaths in their patients. Similarly, Metton and associates [13] reported the largest experience of 3-patch repairs. They found 1 early death in a cohort of 23 children who had 3-patch repairs, although how many of these patients had Williams syndrome is unclear.

An important practical observation of our experience was that higher than normal systemic pressures were necessary in these patients when coming off cardiopulmonary bypass or mechanical support. If these pressures were not achieved, the heart would often fibrillate, necessitating reinstitution of mechanical circulatory support. The exact mechanism of this is unknown; however, we observed that the higher than normal pressures are often required to ensure myocardial perfusion via the thick-walled coronary arteries (Fig 5).

Despite good early results, late mortality and reoperation were significant. Of the 17 Doty repair patients, 4 (24%) died late and 5 (29%) required reoperation up to 23 years after the initial operation. No late deaths or reoperations occurred in the 9 patients who had a 3-patch repair. However, mean follow-up for the 3 patch patients was 5 years compared with almost 15 years in the Doty repair patients. Furthermore, 3 of the 4 late deaths in the Doty repairs occurred at least 3.5 years after the repair, and late reoperation occurred at a mean 11 years after repair. Consequently, we may not yet have seen the late mortality and reoperation with 3-patch repair, and longer follow-up is needed. Thus, direct comparison between surgical techniques is not possible in our study.

Children with Doty repair had longer follow-up. In addition, if techniques were compared, the number of patients in each group would have been small. Furthermore, children with Doty repair had more associated anomalies. Thus, no comparison between the surgical techniques was undertaken. However, late mortality and reoperation was significant in patients who underwent Doty repair. Midterm results of 3-patch repair are encouraging, but longer follow-up is needed.

Our late results of 3-patch repair are similar to those of Metton and colleagues [13], who reported no late deaths or reoperations in 23 patients who had a 3-patch repair

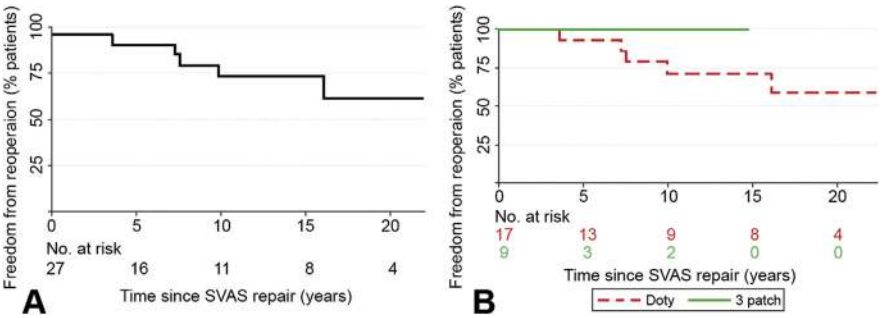

Fig 4. Kaplan-Meier (A) overall freedom from reoperation and (B) freedom from reoperation by Doty (red) and 3-patch repair (green).

Table 5. Reoperation

Repair Type	Reoperation 1	Time Since SVAS Repair (y)	Reoperation 2	Time Since SVAS Repair (y)	Reoperation 3	Time Since SVAS Repair (y)
Doty	Patch enlargement aortic arch	16	None	None	None	None
Doty	Patch enlargement aortic arch, origin innominate artery and distal ascending aorta	3.6	None	None	None	None
Doty	Coarctation repair	7.5	None	None	None	None
Doty	1. Patch enlargement ascending aorta and innominate artery 2. Ascending to descending aorta bypass graft	9.9	1. Repair of restenosis 2. Replace ascending to descending aorta bypass graft	23	None	None
Doty	Konno with St. Jude[a] AVR	7.3	PPM	7.3	Redo Konno, Bentall, and MV repair	16
McGoon	Redo MV repair	16 days	CABG (LITA-LAD) and resection supramitral ring	8.2	None	None

[a] St. Jude Medical, St. Paul, Minnesota.

AVR = aortic valve replacement; CABG = coronary artery bypass graft; LAD = left anterior descending artery; LITA = left internal mammary artery; MV = mitral valve; SVAS = supravalvular aortic stenosis.

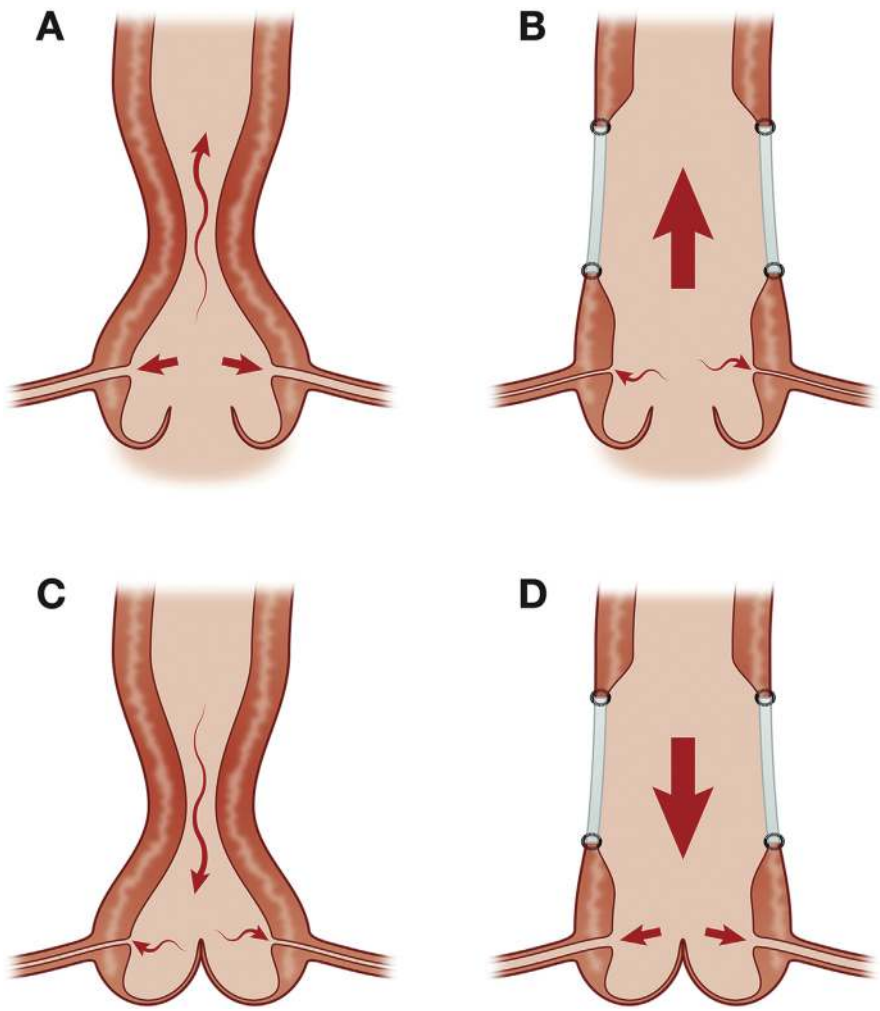

Fig 5. Diagram of the aortic root demonstrates possible dynamic changes in coronary perfusion before and after surgical repair in patients with Williams syndrome. Systole (A) before repair and (B) after repair. Diastole (C) before repair and (D) after repair.

after a mean follow-up of 5 years. However, comparing our results with other studies is difficult because the current studies in the literature are often a mix of different surgical techniques, with an unclear number of patients with Williams syndrome. A multicenter study is necessary to have a reasonable number of patients to compare outcomes of surgical techniques and outcomes of patients with and without Williams syndrome.

A limitation of this study was its retrospective nature. This study covered a long period of time, and changes in treatment might have influenced our outcomes.

In conclusion, surgical repair of SVAS in children with Williams syndrome has excellent early results. However, significant late mortality and morbidity warrant close follow-up.

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