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Altered 4-D magnetic resonance imaging flow characteristics in complex congenital aortic arch repair

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Abstract

Background—Interrupted aortic arch (IAA) is a rare but severe congenital abnormality often associated with bicuspid aortic valve (BAV). Complex re-interventions are often needed despite surgical advances, but the impact of aortic hemodynamics in repaired patients is unknown.

Objective—Investigate effect of IAA repairs on aortic hemodynamics, wall shear stress and flow derangements via 4-D flow MRI.

Materials and methods—We retrospectively analyzed age- and gender-matched cohorts (IAA [$n=6$], BAV alone [$n=6$], controls [$n=6$]) undergoing cardiac MRI including 4-D flow. Aortic dimensions were measured from standard MR angiography. We quantified peak systolic velocities, regurgitant fractions and wall shear stress in the ascending aorta (AAo), transverse arch and descending aorta (DAo) from 4-D flow, and we graded helix/vortex flow patterns from 3-D blood flow visualization.

Results—Children and young adults with IAA had a wide range of arch dimensions, peak systolic velocities, regurgitant fractions and flow grades. Peak transverse arch systolic velocities were higher in people with IAA versus controls ($P=0.02$). Flow derangements in the AAo were found in people with IAA (median grade=2, 5/6 patients, $P=0.04$) and BAV (median grade=3, 5/6 patients, $P=0.03$) versus controls. Flow derangements in the DAo were only seen in people with IAA (median grade=1, 5/6 patients, $P=0.04$), and 5/6 people with IAA had helical flow in head and neck vessels. Wall shear stress was increased in people with IAA along the superior transverse arch and proximal DAo versus controls ($P=0.02$).

Conclusion—Complex congenital aortic arch repairs can change aortic hemodynamics. Associated cardiac defects can further alter findings. Studies are warranted to investigate clinical implications in larger cohorts.

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Conflicts of interest None

Keywords

Aorta; Children; Congenital heart disease; Four-dimensional flow; Heart; Interrupted aortic arch; Magnetic resonance imaging

Introduction

Interrupted aortic arch (IAA) is a discontinuity between two adjacent segments of the aortic arch. It is a rare but severe form of congenital aortic arch anomaly with a prevalence of 5.8 per 100,000 live births, or 0.7% to 1.4% of people with congenital heart disease [1, 2]. IAA is often associated with bicuspid aortic valve (BAV, 32–36%), which is the most common congenital cardiovascular abnormality, affecting 1–2% of the general population [3–7]. In addition, IAA is frequently associated with ventricular septal defects (VSDs, 72%), subaortic stenosis (~25%), common arterial trunk (11%) and DiGeorge syndrome (50–80%) [8–11].

People with IAA typically require neonatal surgical intervention. During the last 20 years, surgeons have preferred a single-stage repair where the entire lesion is addressed in the newborn period by using a homograft or pericardial patch tissue to augment the aorta [10–13]. Prior to this period, surgeons routinely used a multi-stage approach that included placement of an interposition graft between the ascending and descending aorta with a pulmonary artery band in the newborn period and then upsizing the graft to an adult diameter with or without VSD repair at an older age [14]. Regardless of surgical approach, IAA repair is considered complex with a high risk of in-hospital mortality (Society of Thoracic Surgeons and European Association for Cardio-thoracic Surgery mortality score of 4 out of 5) [15]. This mortality score rises to 5 if the IAA is associated with common arterial trunk. Additionally, many people require re-intervention after initial successful IAA repair — 23% with patch augmentation and 54% with interposition graft at 16-year follow-up [10, 11].

Known risk factors for early mortality include younger age, lower birth weight, female gender, earlier era of surgery, and staged palliation; however the underlying mechanisms leading to failure of IAA repair are poorly understood [10]. Recent 4-D flow MRI studies have shown that changes in aortic 3-D blood flow characteristics, such as deranged helix or vortex flow and elevated peak velocities, can be associated with the development of aortic dilation and aneurysms [16, 17]. BAV-mediated changes in aortic outflow characteristics and wall shear stress can result in aortopathy and aortic wall degeneration [18–22]. The use of 4-D flow for surgical planning in a person with IAA was described in a single case study [23], but the impact of complex IAA repair on aortic hemodynamics has not been systematically evaluated.

The aim of this 4-D flow MRI study was to investigate changes in aortic hemodynamics in people with IAA repairs compared to age- and gender-matched patients with BAV alone and healthy controls with trileaflet aortic valves. We hypothesized that the complex architecture of IAA repairs affects hemodynamics beyond BAV-mediated changes and causes flow derangements and wall shear stress alterations downstream of the repairs.

Materials and methods

Study population

We retrospectively queried our 4-D flow database for all patients with the diagnosis of IAA from 2011 to 2018. Six people were found to have repaired IAA (median age = 18 years, interquartile range [IQR] 12–29 years; 3 female). For comparison we chose six age-, body surface area (BSA)- and gender-matched cohorts of patients with BAV alone (median age = 18 years, IQR 16–18 years; 3 female) and with healthy trileaflet aortic valves (median age = 15 years, IQR 14–15 years; 3 female). The BAV alone cohort was also matched for degree of aortic stenosis, aortic regurgitation, and cardiac function. All studies were performed in accordance with our institutional review board (IRB) standards. We obtained informed consent per IRB requirements for the 4-D flow acquisition in patients otherwise undergoing clinically indicated cardiac MRI in this study, which complied with the Health Insurance Portability and Accountability Act.

The type of IAA was defined by clinical chart review: Type A where the interruption occurred at the aortic isthmus between the most distal subclavian artery and the descending aorta, Type B where the interruption occurred between the left common carotid and the left subclavian artery (most common), and Type C where the interruption occurred between the brachiocephalic artery and the common carotid artery.

Magnetic resonance imaging

All subjects underwent standard-of-care cardiothoracic MRI using a 1.5-tesla (T) MRI system (Aera; Siemens, Erlangen, Germany), which included 3-D contrast-enhanced (gadofosveset trisodium 0.03 mmol/kg or gadobutrol 0.15 mmol/kg) MR angiography for quantification of aortic dimensions. Two-dimensional breath-held and electrocardiogram (ECG)-gated cine balanced steady-state free precession (bSSFP) and 2-D phase-contrast MRI were used to assess valve morphology and function. Two-dimensional phase-contrast MRI data were acquired at the level of the aortic valve leaflet tips with single-directional velocity encoding in the through-plane direction. Four-dimensional flow MRI allowed for the in vivo measurement of time-resolved 3-D blood flow velocities with full coverage of the thoracic aorta. Four-dimensional flow MRI consisted of ECG- and respiratory-navigator-gated 3-D time-resolved phase-contrast MRI with three-directional velocity encoding [24–26]. Four-dimensional flow MRI pulse sequence parameters were set based on patient size and peak velocities: repetition time/echo time (TR/TE) = 4.5–5.1/2.4–2.6 ms, field of view = 250–320 mm x 156–244 mm, spatial resolution = 2.0–4.0 x 1.6–2.0 x 1.8–3.0 mm, temporal resolution = 35.7–40.8 ms, velocity sensitivity = 120–400 cm/s, and standard parallel imaging (GRAPPA [generalized autocalibration partial parallel acquisition] technique) had an acceleration factor of R=2. Scan times for 4-D flow were 8–12 min.

Data analysis — aortic dimensions

Thoracic aortic diameters were measured from the 3-D contrast-enhanced MR angiography exams using a dedicated 3-D workstation with multiplanar reformatting capabilities (Vitrea; Vital Images, Minneapolis, MN) per clinical protocol. Maximum orthogonal aortic diameters were measured from inner edge to inner edge based on anatomical landmarks

according to international guidelines at the sinuses of Valsalva, mid-ascending aorta (mid-AAo), distal transverse aortic arch, and descending aorta (DAo) at the level of the left atrium. To account for the range of patient age and body size, aortic z-scores were calculated for each patient based on body surface area (BSA) as defined by the Mosteller equation using EchoIMS (Merge Healthcare, Chicago, IL). Z-scores are not available for descending aorta dimensions, so we used the largest and smallest absolute diameters for comparison.

Data analysis — aortic valve function

To ensure the IAA and BAV cohorts were clinically matched for aortic valve function, we calculated aortic valve peak velocities and aortic regurgitant fractions using the 2-D phase-contrast MRI data in accordance with clinical guidelines [27]. Aortic stenosis grading was based on the peak systolic velocity at the leaflet tips as none (0) = <1.9 m/s, mild (1) = 2.0–2.9 m/s, moderate (2) = 3.0–3.9 m/s, and severe (3) = >4.0 m/s [27]. Aortic valve regurgitation fractions were graded as none (0) = 0%, trace (1) = 0–5%, mild (2) = 5–30%, moderate (3) = 30–50%, and severe (4) = >50% [27].

Data analysis — aortic 4-D flow magnetic resonance imaging

Data analysis included corrections for phase offset errors (eddy currents, Maxwell terms) and velocity aliasing using a home-built tool programmed in MATLAB (MathWorks, Natick, MA). Aortic segmentation using 3-D phase-contrast MR angiography images (Mimics; Materialise, Leuven, Belgium) was used to mask the 4-D flow velocity data and to calculate a peak systolic velocity maximum-intensity projection (MIP), where the maximum peak systolic velocity magnitude was projected onto a sagittal-oblique plane through the thoracic aorta [28]. As illustrated in Fig. 1, we used region-of-interest analysis to quantify aortic peak systolic velocities in the AAo, transverse arch and proximal DAo. We performed regional flow quantification by placing 2-D analysis planes at defined anatomical locations (mid-AAo, distal transverse arch, and DAo at the level of the left atrium) to calculate regurgitant fractions.

We performed aortic blood flow visualization by color-coded 3-D pathlines (EnSight; CEI, Apex, NC). Quantitative evaluation of helicity and vorticity is currently exploratory and a technique for accurate measurement has not been established. For this reason and because of the complexity and diversity of our small patient cohort, helix and vortex secondary flow patterns in the AAo and DAo were graded by a single observer (L.D., 2 years of experience with MR imaging) based on previously reported qualitative methods [29–31]. A 4-point scale was used as follows: none (0) or mild (1) = one 360° turn, moderate (2) = two 360° turns, and severe (3) = three or more 360° turns. Vortex flow was defined as particles revolving around an axis orthogonal to the vessel centerline. Helix flow was defined as particles revolving around the longitudinal axis of the vessel centerline (i.e. corkscrew-like pattern).

Wall shear stress for each cohort was derived from the velocity data for each analysis plane by interpolating the local velocity derivative on the lumen contour using b-splines [32]. Wall shear stress was calculated at 10 segments of the aortic wall including the AAo, transverse arch and DAo.

Statistics

Patient characteristics are summarized using descriptive statistics that include means, standard deviations, medians and interquartile ranges. We used Wilcoxon rank sum testing to compare aortic stenosis and regurgitation grading between IAA and BAV groups. Comparisons among all three groups were based on either analysis of variance (ANOVA) or Kruskal-Wallis H testing, as appropriate. A two-sided P -value <0.05 was considered statistically significant. If significance was found, we performed post hoc pairwise testing via t -testing or Tukey and Kramer (Nemenyi) all-pairs test with Tukey-Dist approximation. All statistical analysis was performed in R [33, 34].

Results

Comparison of cohorts

Age-, gender- and BSA-matched analysis showed an increased mid-AAo diameter z-score in the BAV group versus controls ($P=0.04$). No other differences between arch diameters were found (Table 1). Figure 1 shows a comparison of aortic peak velocity MIPs in a representative subject for each of the three cohorts (IAA, BAV, controls). The patients with IAA and BAV had elevated peak velocities in the AAo compared to the control patient (Fig. 1). IAA repair also resulted in complex high-velocity flow jet patterns in the transverse arch and proximal DAo (Fig. 1). These findings were supported by data from the entire study population, summarized in Table 2. Peak systolic flow velocity in the transverse arch was increased in the IAA cohort when compared to normal controls ($P=0.02$). There were no statistically significant differences in the regurgitant fractions between groups (Table 2).

Figure 2 shows a comparison of 3-D flow streamline visualizations in a representative subject for each of the three cohorts (IAA, BAV, controls). Aortic blood flow patterns can be visualized via 3-D pathline videos for these patients in Supplementary Online Resource 1. In the patient with IAA, substantial helix and vortex flow derangement can be seen in the AAo and DAo (Fig. 2, Supplementary Online Resource 1). In comparison, flow derangement in the patient with BAV was confined to the AAo, while the control subject had no flow derangement. Cumulative findings of flow derangement across all cohorts are summarized in Table 2. Flow derangement in the AAo was found in patients with both IAA (median grade=2, 5/6 patients, $P=0.04$) and BAV (median grade=3, 5/6 patients, $P=0.03$) compared to normal controls. The one IAA patient without AAo flow derangement had a trileaflet aortic valve. Flow derangement in the DAo was only seen in patients with IAA (median grade=1, 5/6 patients) compared to patients with BAV and normal controls, with $P=0.04$ in both pairwise comparisons.

Figure 3 shows a comparison of mean wall shear stress values among the groups for all 10 regions analyzed. Wall shear stress was increased along the superior transverse arch near the head and neck vessels (Region 5), posterior proximal DAo (Region 7) and anterior proximal DAo (Region 8) in the patients with IAA compared to controls ($P=0.02$ for all).

Interrupted aortic arch cohort — detailed analysis

The patients with IAA had different surgical repairs based on age and presence of other cardiac defects (Table 3). Only one patient had IAA Type A. All other patients had Type B. Patients A–C had multi-stage repairs using conduits, whereas patients D–F had single-stage neonatal repairs without conduits. All 6 patients had VSDs, 5 had BAV, 3 had atrial septal defects (ASDs) and 4 had DiGeorge syndrome.

Figure 4 shows a side-by-side comparison of systolic blood flow patterns (3-D streamlines) and aortic geometry (surface-rendered 3-D MR angiography) for all six patients with IAA. Flow derangement was seen in the DAo in 5/6 patients with IAA. The top row (Fig. 4, Patients A–C) illustrates the older patients in the cohort (29, 29 and 18 years). These patients underwent multi-stage repair with conduits/tube grafts. Patient A underwent three conduit revisions before 8 years of age and had flow derangements in both the AAo and DAo. Patient B required only one conduit revision, at 10 years of age, and was the only patient who did not have flow derangement in the DAo. Patient C also had only one conduit replacement, but she had been lost to follow-up and presented with significant flow derangement throughout the arch. Patient C's flow visualization also suggested retrograde blood supply to the head and neck vessels via the very hypoplastic residual native arch. The bottom row (Fig. 4, Patients D–F) illustrates the younger patients in the cohort (17, 13, and 11 years). These patients underwent single-stage neonatal repair without conduits and had less flow derangement in the DAo compared to the older Patients A and C. Patient D was the only patient with IAA who had a normal trileaflet aortic valve and without flow derangement in the AAo. There was also suggestion of helical flow in the head and neck vessels for Patients A, B, C, E and F. Aortic blood flow patterns can be visualized via 3-D pathline videos for all patients with IAA, in Supplementary Online Resource 2.

There was a wide range of aortic arch dimensions, peak systolic velocities, regurgitant fractions, and flow grades among the patients with IAA (Tables 4 and 5). Patient E had subaortic stenosis requiring two surgeries after initial IAA repair and had the highest peak systolic velocity (3.0 m/s) and a high degree of flow derangement (flow grade = 4) in the AAo. Patient C had the smallest transverse arch/conduit diameter z-score and had the highest transverse arch and DAo peak systolic velocities (3.4 m/s and 3.3 m/s); this patient also had the most severe flow derangement in the DAo (flow grade = 6).

Discussion

This study demonstrates that complex repair of IAA, which is a rare but severe congenital aortic arch abnormality, can result in overt alterations of aortic hemodynamics. The importance of MRI surveillance in patients with IAA has been discussed [35], only one case report in the literature has evaluated 4-D flow in a patient with IAA [23]. In that case, the 4-D flow analysis allowed clinicians to correctly evaluate the complex anatomy and flow parameters in various regions of interest and use the data for surgical planning via a left lateral thoracotomy with pulmonary artery and femoral artery cannulation versus a more invasive median sternotomy. Because 4-D flow data can be analyzed retrospectively, it can allow clinicians flexibility when planning care. Although echocardiography can be used to assess velocities at specific points, accuracy depends on operator experience, and many

calculation assumptions are made in patients with complex anatomy and multi-level stenosis. Four-dimensional flow allows for analysis in all directions within a volume of image acquisition and is time-resolved to provide a more comprehensive quantification of velocities in multiple regions. The MIP methodology used in our study allows for a high-resolution voxel-by-voxel analysis within a region of interest [28]. Four-dimensional flow also offers additional benefits, particularly in patients with complex disease, by allowing visualization of flow derangements after repair and evaluation of advanced parameters like wall shear stress to better understand potential clinical complications in the future.

In our study, the greatest difference in flow characteristics between the IAA versus BAV and control groups was the presence of flow derangement in the DAo. The severity of flow derangement varied among patients with IAA, which was likely caused by differences in how each patient's surgical repair affected flow downstream of the graft. For example, Patients A and C had large conduits/interposition grafts and appeared to have more severe flow derangement in the DAo. The younger patients — D, E and F — had single-stage repairs and less severe qualitative flow disturbances in the DAo, possibly because of improvement in surgical approach or a shorter time period for manifestation. Additionally, wall shear stress along the proximal DAo was increased in the IAA cohort when compared to controls, which suggests need for long-term monitoring for aortopathy in this region after IAA repair. Patients with even simple coarctations have been shown to develop aneurysms near their sites of repair [36]. The possible correlation of wall shear stress to development of aneurysms in this region should be evaluated in larger cohorts.

Peak systolic flow velocities in the transverse arch were increased in the IAA cohort compared to controls. Literature has shown that patients with BAV with coarctation repair have higher peak systolic velocities in the transverse arch compared to those with BAV alone (1.4 m/s versus 1.0 m/s, $P<0.01$) [21]. This might be because of the characteristics of repair in this region, including variable conduit sizes and number of surgeries. For example, Patient C had the smallest transverse arch/conduit diameter z-score and had the highest transverse arch peak systolic flow velocity. There was also increased wall shear stress along the superior transverse arch near the head and neck vessels of the patients with IAA compared to controls, suggesting a relationship between peak systolic velocities and wall shear stress. Interestingly, there was suggestion of flow derangement, particularly helical flow, in the visualized head and neck vessels of the patients with IAA (Fig. 4). In addition to Patient C's hypoplastic conduit size, the head and neck vasculature appeared to be supplied by retrograde flow via the very hypoplastic residual native arch. Although this could suggest a re-intervention is needed to increase the size of the surgical conduit in this patient, the actual clinical implication of flow derangement in the head and neck vessels is somewhat unclear. It might be an important postoperative factor to consider when evaluating neurologic outcomes in this patient population. Literature has extensively evaluated the neurodevelopmental morbidity in patients with congenital heart disease including arch abnormalities, but it has focused on the prenatal, demographic and perioperative factors that affect long-term neurologic outcomes [37]. Studies have also shown an increased prevalence of intracranial aneurysms in patients with BAV and aortic arch abnormalities, and this prevalence is even greater if these anomalies are present together [38, 39]. More detailed imaging of head and neck vasculature should be considered in future 4-D flow studies in

patients with complex aortic arch repairs, with correlation of the findings to potential morbidities.

Elevated peak systolic velocities and flow derangements in the AAo of the IAA and BAV cohorts compared to controls were likely related to the presence of BAV in 5/6 patients with IAA. This is illustrated by Patient D having a trileaflet aortic valve and a normal peak systolic flow velocity in the AAo, no helix or vortex flow in the AAo, and the smallest aortic root and mid-AAo diameter among the patients with IAA (Fig. 4, Tables 4 and 5). It is further supported by previous literature showing AAo flow abnormalities in patients with BAV [19–21]. Similar to the trend in our findings, in Allen et al. [21], the peak systolic velocity in the AAo of patients with BAV was 1.3 ± 0.4 m/s, which was higher than in the transverse arch (1.1 ± 0.3 m/s) and DAo (1.0 ± 0.2 m/s). In Bissell et al. [19], 76% of patients with BAV had helical flow derangement in the AAo ($n=72/95$), 13% had “complex flow” in the AAo ($n=12/95$) and 36% had helical flow derangement in the DAo ($n=34/95$). All but one patient with BAV in our study, both in the IAA and isolated BAV cohorts, had flow derangements in the AAo, and no patients had flow derangements in the DAo.

Other associated cardiac defects in patients with IAA might also lead to flow abnormalities, such as Patient E’s clinically significant subaortic stenosis requiring two additional surgeries. In addition to this patient’s BAV, the subaortic stenosis was likely the cause of his increased AAo peak systolic velocity and flow derangement in comparison to the other patients with IAA. Because IAA is typically accompanied by other cardiac defects, it would be clinically beneficial to determine the severity of their effects on arch characteristics in future studies.

Although MRI is becoming a consistent tool for surveillance in patients with repaired congenital heart disease, the main limitation of our study is the small number of patients available for analysis because of the diversity and complexity of aortic arch pathology and surgical management. This makes it difficult to assemble a large cohort of patients and limits the ability to draw quantitative conclusions. Additionally, because our patients typically had only one MRI for evaluation, another limitation is the lack of longitudinal data to review changes in the assessed parameters and to determine the effect of hemodynamic alterations on patient outcomes. Our study provides initial observations and demonstrates feasibility of 4-D flow analysis that can guide larger prospective studies.

Conclusion

IAA repair is complex and has varying effects on aortic arch characteristics, including flow derangements and increased wall shear stress in the DAo downstream of repair as hypothesized, increased peak systolic flow velocities and wall shear stress in the transverse arch, and suggestion of flow derangements in the head and neck vessels. Associated cardiac defects, including BAV and subaortic stenosis, can further alter these findings. Because of the small cohort size of this feasibility study, comparison of quantification parameters was somewhat limited. Future studies are warranted to investigate the clinical impact of these changes associated with congenital aortic arch abnormalities in larger cohorts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Representative maximum-intensity projections (MIPs) of aortic peak systolic velocities in the ascending aorta (AAo; region of interest [ROI] 1), transverse arch (ROI 2) and descending aorta (DAo; ROI 3) with a color bar representing the velocity range in m/s, in (a) an 18-year-old woman with interrupted aortic arch (IAA) + bicuspid aortic valve (BAV) with right and left cusp fusion, status post AAO–DAo interposition Gortex graft repair at <30 days of age and at 1 year of age; (b) a 13-year-old boy with BAV with right and non-cusp fusion, no prior surgeries; and (c) a 14-year-old female healthy control with trileaflet aortic valve

Fig. 2.

Three-dimensional MRI streamline images compare secondary flow patterns in the aortic arch in an (a) 18-year-old woman with interrupted aortic arch (IAA) + bicuspid aortic valve (BAV), 17 years post repair, with mild helix and severe vortex flow in the ascending aorta (AAo) and severe helix and vortex flow in the descending aorta (DAo); (b) 13-year-old boy with BAV, no prior surgeries, moderate helix and mild vortex flow in the AAo, no flow derangement in the DAo; and (c) a 14-year-old female control patient with no helix or vortex flow. See Supplementary Online Resource 1 for 3-D pathline flow visualizations for each of these patients

Fig. 3.

Wall shear stress images show regions of analysis for interrupted aortic arch (IAA; **a**), bicuspid aortic valve (BAV; **b**) and control (**c**) cohorts. The mean and standard deviation at each region for all patients in the cohort is provided under each image. Asterisks indicate regions that showed statistically significant differences between patients with IAA and controls

Fig. 4.

Three-dimensional MRI streamline images and 3-D reconstructions for patients with interrupted aortic arch (IAA) show a wide range of flow derangements. **a–f** Patient A (**a, b**), a 29-year-old man; Patient B (**c, d**), a 29-year-old woman; and Patient C (**e, f**), an 18-year-old woman, were the older patients in the cohort and were thus part of an earlier surgical era. They underwent multi-stage repair with conduits/tube grafts (**b, d, f**). Patient A had helix and vortex flow derangement in the ascending aorta (AAo), helix flow in the descending aorta (DAo) and suggestion of helix flow in the head and neck vessels (**a**). Patient B was the only patient without flow derangement in the DAo (**c**). Patient C had the greatest degree of flow derangement in the DAo, with both helix and vortex flow and suggestion of retrograde blood flow to the head and neck vessels via a residual hypoplastic native arch (**e**). **g–l** Patient D (**g, h**), a 17-year-old girl; Patient E (**i, j**), a 13-year-old boy; and Patient F (**k, l**), an 11-year-old boy, were the younger patients in our cohort and thus underwent single-stage neonatal repairs (**h, j, l**). They had less helix flow and no vortex flow derangement in the DAo (**g, i, k**). Patient D was the only patient with a trileaflet aortic valve, without AAo flow derangement and without clear helix flow in the head and neck vessels (**g**). Patient E had subaortic stenosis requiring two surgical interventions after initial aortic arch repair and had the highest flow velocity in the AAo (**i**). Patient F had helix flow in both the AAo and DAo (**k**). See Supplementary Online Resource 2 for 3-D pathline flow visualizations for each patient with IAA.

Table 1

Comparison of patient characteristics, aortic valve function and arch dimensions

	IAA ^a n=6	BAV ^a n=6	Control (TAV) ^a n=6	P-value ^b
Age	18 (12–29)	18 (16–18)	15 (14–15)	0.24
Male/female	3/3	3/3	3/3	-
BSA (m ²)	1.5 (1.0–1.8)	1.6 (1.3–2.0)	1.6 (1.5–1.7)	0.68
Aortic stenosis grade	0.5 (0–2)	0 (0–1)	-	0.41 ^c
Aortic regurgitation grade	1 (0–2)	1 (1–2)	-	0.93 ^c
Aortic root z-score	2.3 (0.2–4.8)	2.9 (1.5–3.7)	1.1 (0.8–1.7)	0.39
Mid-AAo z-score	2.0 (–0.3–7.2)	3.1 (1.4–5.3)	–0.1 (–0.5–0.7)	0.04
Transverse arch z-score	–0.5 (–2.3–3.7)	0.3 (–.9–1.1)	0.3 (–0.2–0.7)	0.96
DAo dimension max (mm)	17 (11–23)	18 (16–19)	17 (15–19)	0.98
DAo dimension min (mm)	15 (10–20)	16 (14–18)	15 (14–17)	0.64

^aValues are reported as median (interquartile range)^bA two-sided *P*-value <0.05 was considered statistically significant (bold values)^cComparing IAA and BAV groups only

AAo ascending aorta, BAV bicuspid aortic valve, BSA body surface area, DAo descending aorta, IAA interrupted aortic arch, TAV trileaflet aortic valve

Table 2

Comparison of aortic arch velocities, regurgitant fractions and flow characteristics

		IAA ^a n=6	BAV ^a n=6	Control (TAV) ^a n=6	P-value ^b
Peak systolic velocity (m/s)	AAo	1.7 (1.4–2.4)	1.9 (1.7–2.2)	1.4 (1.3–1.6)	0.06
	Trans arch	1.8 (1.3–2.5)	1.5 (1.4–1.6)	1.2 (1.1–1.3)	0.02
	DAo	1.6 (1.3–2.5)	1.6 (1.4–1.6)	1.4 (1.2–1.5)	0.17
Regurgitant fraction (%)	AAo	7.2 (1.1–24.8)	1.2 (0.6–2.5)	0.4 (0.3–1.4)	0.07
	Trans arch	3.6 (1.0–14.9)	2.8 (0–5.6)	3.0 (0.5–4.1)	0.69
	DAo	9.3 (1.7–14.3)	3.8 (0.5–8.0)	2.7 (0.1–5.1)	0.36
Composite flow derangement ^c	AAo	2 (1–4)	3 (2–3)	0	0.01
	DAo	1 (1–4)	0	0	<0.01

^aAll values are reported as median (interquartile range)^bA two-sided *P*-value <0.05 was considered statistically significant (bold values)^cHelix plus vortex grades in each region

AAo ascending aorta, BAV bicuspid aortic valve, DAo descending aorta, IAA interrupted aortic arch, TAV trileaflet aortic valve, Trans arch transverse aortic arch

Table 3

Interrupted aortic arch patient characteristics and surgical history

Patient	Age (yrs)	Gender	IAA type	BAV type	Other cardiac defects	Surgeries (age at repair)
A	29	M	B	Right/left	VSD, subaortic stenosis	1. 6-mm PA–DAo Impra conduit + PA band (11 days) 2. Relocation of original conduit to AAo–DAo + VSD repair (6 months) 3. 8-mm left carotid–DAo Gortex conduit (22 months) 4. AAo–DAo conduit revision to #18 hemashield tube graft (8 years)
B	29	F	B	*	ASD, VSD	1. Aao–Dao #8 Gortex conduit (5 days) 2. Aao–Dao #16 Hemashield tube graft + ASD repair (10 years) 3. Ross Konno procedure with #23 pulmonary homograft (16 years) 4. #32 valve-sparing aortic root replacement + RV–PA conduit (28 years)
C	18	F	B	Right/left	VSD	1. AAo–DAo interposition graft (<1 month) 2. VSD repair (1 month) 3. AAo–DAo interposition graft replacement (1 year)
D	17	F	A	N/A	VSD	1. IAA primary repair + VSD repair (7 days)
E	13	M	B	Right/left	ASD, VSD, subaortic stenosis	1. IAA primary repair + VSD and ASD repair (1 month) 2. Subaortic fibromuscular resection (2 years) 3. Modified Konno subaortic resection (8 years)
F	11	M	B	Right/left	VSD	1. IAA repair via direct anastomosis + VSD repair (11 days) 2. Suspension of innominate artery to posterior sternum (6 months)

* Patient B had BAV prior to Ross surgery, type unknown

AAo ascending aorta, ASD atrial septal defect, BAV bicuspid aortic valve, DAo descending aorta, F female, IAA interrupted aortic arch, M male, N/A not available, PA pulmonary artery, RV right ventricle, VSD ventricular septal defect, yrs years

Table 4

Detailed quantification for patients with interrupted aortic arch

Patient	Age	BSA	AS ^b	AR ^c	Root	Aortic dimension Z-score ^a			Peak systolic velocity (m/s)			Regurgitant fraction (%)		
						AAo	Trans arch	DAo	AAo	Trans arch	DAo	AAo	Trans arch	DAo
A	29	1.8	1	1	+4.7	+2.6	-2.2	1.5	2.3	1.8	1.5	24.4	3.4	14.3
B	29	1.7	0	2	+1.1	+4.1	+1.2	0.9	1.1	1.2	0.9	10.0	13.8	14.3
C	18	1.3	2	3	+5.2	+16.6	-2.6	3.3	1.7	3.4	3.3	26.0	18.0	12.8
D	17	1.9	0	1	-0.6	-1.8	-2.2	2.2	1.7	1.9	2.2	0	3.8	5.7
E	13	1.0	3	0	+0.5	+0.2	+5.3	1.7	3.0	2.2	1.7	1.4	1.2	0
F	11	0.9	0	0	+3.5	+1.4	+3.2	1.5	1.5	1.4	1.5	4.4	0.2	2.3
Median (IQR)	18 (12–29)	1.5 (1.0–1.8)	0.5 (0–2)	1 (0–2)	2.3 (0.2–4.8)	2.0 (-0.3–7.2)	-0.5 (-2.3–3.7)	1.6 (1.3–2.5)	1.7 (1.4–2.4)	1.8 (1.3–2.5)	1.6 (1.3–2.5)	7.2 (1.1–24.8)	3.6 (1.0–14.9)	9.3 (1.7–14.3)

^aZ-scores were not available for descending aorta (DAo) dimensions^bAortic stenosis (AS) grading scale: none (0) = <1.9 m/s; mild (1) = 2.0–2.9 m/s; moderate (2) = 3.0–3.9 m/s; severe (3) = >4.0 m/s^cAortic regurgitation (AR) fraction scale: none (0) = 0%; trace (1) = 0–5%; mild (2) = 5–30%; moderate (3) = 30–50%; severe (4) = >50%
AAo ascending aorta, BSA body surface area, DAo descending aorta, IQR interquartile ratio, Trans arch transverse arch

Table 5

Flow grades for patients with interrupted aortic arch

Patient	Age	BSA	Helix flow grade ^a		Vortex flow grade ^a		Composite flow derangement (helix+vortex grades)	
			AAo	DAo	AAo	DAo	AAo	DAo
A	29	1.8	2	3	1	0	3	3
B	29	1.7	0	0	1	0	1	0
C	18	1.3	1	3	3	3	4	6
D	17	1.9	0	1	0	0	0	1
E	13	1.0	1	1	3	0	4	1
F	11	0.9	1	1	0	0	1	1
Median (IQR)	18 (12–29)	1.5 (1.0–1.8)	1 (0–1)	1 (1–3)	1 (0–3)	0 (0–1)	2 (1–4)	1 (1–4)

^aFlow grade: none (0); mild (1) = one 360° turn; moderate (2) = two 360° turns; severe (3) = three or more 360° turns

AAo ascending aorta, BSA body surface area, DAo descending aorta, IQR interquartile range