Head and Neck Vessel Size by Angiography Predicts Neo-Aortic Arch Obstruction After Norwood/Sano Operation for Hypoplastic Left Heart Syndrome

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ABSTRACT: Objectives. To identify and predict neo-aortic arch obstruction (NAAO) in children after Norwood/Sano operation (NO) for hypoplastic left heart syndrome (HLHS). **Background.** NAAO is associated with morbidity and mortality after NO for HLHS and no objective measure has predicted the initial occurrence of NAAO. Computational flow models of aortic coarctation demonstrate increased wall shear stress (WSS) in vessels proximal to the coarctation segment, which we believe also occurs with NAAO. These vessels respond by increasing their luminal diameter to maintain normal WSS. We hypothesized that the relative increase in diameters of head and neck vessels to the isthmus, as measured by angiography, would identify hemodynamically significant NAAO and predict future NAAO. **Methods.** Retrospective review of patients with HLHS and at least one catheterization with aortic angiography after NO. Diameters of head and neck vessels were totaled and divided by the isthmus diameter to give a head and neck index (HNI), which was compared to coarctation index (CI) for identifying and predicting future NAAO. **Results.** Forty-four patients were identified, 17 with and 27 without NAAO. Receiver operator characteristic analysis using a value for CI ≤0.5 showed a sensitivity of 47% and specificity of 89%. For HNI, a value >2.65 gave a sensitivity of 77% and specificity of 93%. Three patients who developed NAAO after their initial catheterization had CI >0.5, but abnormally high HNI >2.65. **Conclusions.** HNI is a more robust indicator of hemodynamically significant NAAO than CI and may predict its future occurrence after NO for HLHS.

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Hypoplastic left heart syndrome (HLHS) is one of the most complicated congenital heart lesions that pediatric cardiologists and congenital heart surgeons treat. A recent review of the current status of patients with HLHS highlights the significant morbidity and mortality associated with neo-aortic arch obstruction (NAAO) after Stage I palliative surgery.[1] NAAO has been noted to occur in up to 37% of patients after the Norwood operation (NO)[2] and was identified as the cause of death in 14% of patients after NO in an autopsy series.[3] Identifying residual anatomic lesions and addressing them early reduces interstage mortality.[4]

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Catheter-based balloon aortoplasty of NAAO has become the first-line therapy, with success approaching 100%,[5] but it has been difficult to identify patients at risk of developing obstruction. Porras and colleagues reviewed their experience with balloon aortoplasty for NAAO following NO and identified factors associated with recurrence following initial balloon angioplasty, including proximal arch obstruction, age less than 3 months at intervention, and smaller pre-intervention coarctation index (CI).[2] To date, there has been no reliable method to identify at-risk patients before they develop NAAO.

Computational flow models have been developed to study different congenital heart defects, including coarctation of the aorta.[6-8] LaDisa and colleagues recently published computation flow models of coarctation of the aorta, which include measures of wall shear stress (WSS) and show a marked elevation of WSS to more than twice the normal range of 10 to 20 dynes/cm^2 in the head and neck vessels proximal to the coarctation.[7] Numerous studies have shown that to maintain WSS in a normal range, blood vessels respond with intimal proliferation and increased luminal diameter.[9-12]

Based on these findings in patients with simple coarctation of the aorta, we hypothesized that similar changes occur in the proximal head and neck vessels in patients with NAAO after NO for HLHS and that these changes could be assessed by measuring the ratio of the diameters of the head and neck vessels to the narrowest region of the neo-aortic arch. We then tested the hypothesis that this ratio could be used to identify hemodynamically significant NAAO and to predict its future occurrence in patients with HLHS after NO.

Methods

We retrospectively identified patients with HLHS who had at least one catheterization with aortic angiography after NO from 2002 through 2011. Data collected for all catheterizations included demographics, hemodynamics, aortic arch branching pattern, measurements of the diameters of all head and neck vessels proximal to the isthmus, narrowest portion of the isthmus and the descending aorta at the diaphragm, or the most distal portion visible in the angiogram (Figure 1). For patients with NAAO who underwent balloon aortoplasty, measures of the isthmus and descending aorta were repeated post intervention. All measurements were made from lateral projections of aortic angiograms.

The diameters of the head and neck vessels were totaled and divided by the narrowest diameter of the aortic isthmus to give a head and neck index (HNI). A higher HNI was considered indicative of possible NAAO. For comparison, two other measures

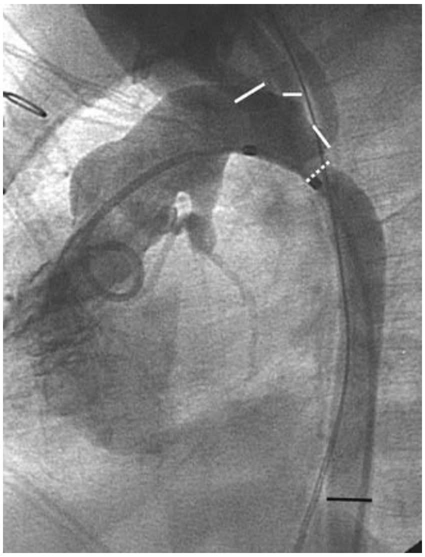

Figure 1. *Representative lateral projection aortic angiogram showing the location of measurements for head and neck vessels (solid white lines), narrowest portion of the isthmus (dashed white line), and descending aorta at the diaphragm (black line).*

were calculated: (1) coarctation index (CI), by dividing the narrowest diameter of the isthmus by the descending aorta at the diaphragm; and (2) the narrowest diameter of the isthmus indexed to body surface area (Isth). A value ≤0.5 was used to define a significantly small CI, as used by Porras and colleagues;[2] smaller values of Isth were considered indicative of possible NAAO.

Two groups were established: patients who never developed NAAO (NoObs) and patients who either had NAAO at their first catheterization or developed NAAO on subsequent catheterizations (Obs).

Continuous, normally-distributed variables are presented as mean ± standard deviation and were compared using student's t-test. Non-normally distributed data are presented as median (interquartile range) and were compared using Mann-Whitney U-test. Receiver operating characteristic (ROC) curve was used to test the sensitivity and specificity of HNI, CI, and Isth for identifying patients who develop NAAO. Negative and positive predictive value (NPV and PPV) were also determined for all three measures. A *P*-value <.05 was considered statistically significant. The Institutional Review Board at the University of Virginia reviewed this protocol and waived the need for informed consent.

Results

Forty-four patients with HLHS underwent NO and had at least one catheterization with aortic angiography postoperatively, with 27 in the NoObs group and 17 (39%) in the Obs group. Patient characteristics at the time of initial catheterization are shown in Table 1. NoObs patients were older and bigger at the time of catheterization and had lower mean branch pulmonary artery pressures. There was no difference in right ventricular systolic pressure (RVSP) or mean atrial pressures, and a non-significant trend toward lower right ventricular end-diastolic pressure (RVEDP) in the NoObs group (Table 1). CI and Isth were higher and HNI was lower in the NoObs group.

Table 2 shows the different aortic branching patterns found in our patients. All patients had left-sided aortic arches and nearly 25% had non-normal branching patterns.

ROC analysis using a value for CI ≤0.5 showed an area under the curve (AUC) of 0.871 (*P*<.001), a sensitivity of 47% and specificity of 89%; PPV was 73% and NPV was 73%. For HNI, a value >2.65 gave an AUC of 0.81 (*P*=.001), sensitivity of 77% and specificity of 93%; PPV was 87% and NPV was 86%. For Isth, a value ≤16.5 mm/m^2 gave an AUC of 0.797 (*P*=.001), sensitivity of 71% and specificity of 82%; PPV was 71% and NPV was 82%. To achieve a similar sensitivity to HNI, the analysis for CI was repeated with the cut-off increased to 0.63, which gave a sensitivity of 77% and specificity of 78%; PPV was 68% and NPV was 84%.

Of the 17 patients with NAAO, 14 (82%) underwent catheter-based balloon angioplasty, 6 with 1 recurrence and 1 with 2 recurrences after initial angioplasty.

Three patients who did not have NAAO at the time of their initial catheterization subsequently developed it, and their details are shown in Table 3. At the time of initial catheterization, none had hemodynamically significant gradients across their aortic arch, and all three had CI >0.5 and only 1 patient had an Isth <16.5. However, all 3 had HNI greater than the cut-off of 2.65 and developed NAAO 6 to 11 weeks after initial catheterization. Two required catheter-based intervention; the third had obstruction that was not felt to be amenable to balloon angioplasty by the attending interventionalist.

Discussion

Our study demonstrated that HNI is superior to CI or Isth for identifying patients with hemodynamically significant NAAO after NO for HLHS. Further, an elevated HNI may be a predictor of future NAAO. Because of the invasive nature of angiography to obtain the aortic measurements, this is not a perfect method for early detection of NAAO in all patients. However, it is information that can be obtained easily without any further risk to patients already undergoing catheterization as part of their pre-operative assessment for Stage 2 palliative surgery.

It could be argued that since most of the patients in whom we identified NAAO underwent balloon aortoplasty during the same catheterization, HNI is not a predictive measure. However, measurements of CI taken from the same angiograms were not as robust at identifying these patients as having NAAO requiring intervention, and the mean CI for the patients undergoing NAAO intervention was higher than the previously used cut-off of 0.5.[2] In addition, all 3 patients who developed NAAO after their initial catheterization would not have been identified using a CI <0.5, but all 3 had abnormally high HNI and developed NAAO within 3 months.

Interestingly, simply measuring the diameter of the isthmus was not as robust as HNI at identifying NAAO. This may imply that when arch obstruction is hemodynamically significant, not only is the isthmus narrowed, but there is also proximal head and neck vessel dilation, similar to the computational flow models of simple coarctation.[7]

Our patients had a variety of branching patterns for the head and neck vessels, including some with 3 head and neck vessels and a vertebral artery arising directly from the aorta and some with only 2 head and neck vessels arising from the aorta, but this did not seem to affect the predictive ability of the HNI. Given that vessels proximal to a narrowed segment of the aortic arch have been shown to have increased WSS,[7] it is expected that they will dilate to attempt to normalize WSS, regardless of the number of vessels present.[9-12]

The invasive nature of catheter-based angiography may prohibit the routine use of HNI for identifying asymptomatic NAAO, but it could be possible to perform a similar measure using two-dimensional echocardiography or cardiac magnetic resonance imaging (CMR). There may be limitations in obtaining an HNI by echocardiography because of poor acoustic windows from prior surgical intervention and small patient size. On review of serial echocardiograms obtained prior to the first catheterizations in our study group, 13 patients (30%) had inadequate visualization of the aortic arch and head and neck vessels to perform a non-invasive measure of HNI. However, we are currently investigating the utility of strain analysis on apical 4-chamber echocardiographic images for non-invasive markers of NAAO that could be detected earlier. Non-invasive imaging with CMR should provide excellent visualization of the aortic arch and head and neck vessels, and the potential addition of protocols to assess flow and WSS may increase the ability to identify patients at risk for developing NAAO before they experience hemodynamic deterioration.

Study limitations. This study was limited by its single-center, retrospective design. Since the initial work was completed, we have begun prospectively evaluating the utility of HNI for identifying patients at risk for NAAO after pre-stage 2 catheterization. In addition, we are evaluating the utility of HNI for identifying hemodynamically significant NAAO in patients from a second institution.

Conclusions. Routine use of HNI may help determine which patients have hemodynamically significant NAAO after NO for HLHS requiring intervention. In addition, HNI may have value in identifying patients at risk to develop future NAAO. This measure will require more robust testing in prospective, multi-institutional studies before recommendations can be made for the utility in all patients after NO for HLHS.

Table 1. Patient characteristics at the time of initial catheterization in the NoObs (n = 27) and Obs (n = 17) groups.

Characteristic	NoObs	Obs	*P*
Age (days)	144 ± 35	98 ± 44	<.001
Weight (kg)	5.79 ± 1	4.51 ± 0.83	<.001
RPA mean pressure (mm Hg)	13.2 ± 3	15.9 ± 4.6	.05
LPA mean pressure (mm Hg)	14.5 ± 4.1	18.9 ± 5.6	.013
RA mean pressure (mm Hg)	7 (4.8, 9)	8 (5.3, 10.5)	NS
LA mean pressure (mm Hg)	7.5 (5, 10)	8 (6, 11)	NS
RVSP (mm Hg)	85 (78, 90)	82 (65.5, 101)	NS
RVEDP (mm Hg)	8 (6, 11)	10 (8, 15.5)	.057
Arch gradient	0 (0, 1)	19 (10, 30)	<.001
CI	0.88 ± 0.17	0.60 ± 0.18	<.001
HNI	2.23 ± 0.43	3.46 ± 1.59	.006
Isth (mm/m^2)	19.97 ± 4.08	14.29 ± 5.07	<.001

RPA = right pulmonary artery; LPA = left pulmonary artery; RA = right atrium; LA = left atrium; RVSP = right ventricular systolic pressure; RVEDP = right ventricular end-diastolic pressure; CI = coarctation index; HNI = head and neck vessel index; Isth = isthmus diameter indexed to body surface area.

Table 2. Aortic arch sidedness and head and neck vessel branching patterns.

Arch-Sidedness	Branching Pattern	N (%)
Left	Right innominate, left carotid, left subclavian	34 (77%)
Left	Left carotid/right innominate common origin, left subclavian	3 (7%)
Left	Common carotid origin, left subclavian, aberrant right subclavian	1 (2%)
Left	Left carotid off right innominate, left subclavian	1 (2%)
Left with right descent	Left innominate, right carotid, right subclavian	1 (2%)
Left	Left subclavian, common origin of carotids, right subclavian	1 (2%)
Left	Right innominate, left carotid, no left subclavian	1 (2%)
Left	Right innominate, left carotid, vertebral, left subclavian	1 (2%)
Left	Left carotid/right innominate common origin, vertebral, left subclavian	1 (2%)

Table 3. Characteristics of three patients who had no NAAO on initial catheterization and developed subsequent NAAO. Patients 1 and 2 underwent aortic intervention for their NAAO.

Patient	Initial Gradient (mm Hg)	CI	HNI	Isth (mm/m^2)	Days Until Coarctation	Coarctation Gradient (mm Hg)
1	6	0.62	2.66*	18.10	42	80
2	0	0.83	2.72*	19.20	77	23
3	6	0.75	2.87*	15.59	55	15

**denotes head and neck vessel index (HNI) that would indicate NAAO.*
CI = coarctation index; Isth = isthmus diameter indexed to body surface area.

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