Significant correlation of comprehensive Aristotle score with total cardiac output during the early postoperative period after the Norwood procedure

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Background: The comprehensive Aristotle score has been proposed as an individualized measure of the complexity of a given surgical procedure and has been reported to significantly correlate with postoperative morbidity and mortality after the Norwood procedure. An important factor leading to postoperative morbidity and mortality is low cardiac output. We studied the correlation between the comprehensive Aristotle score and cardiac output (CO) in infants after the Norwood procedure.

Methods and Results: Respiratory mass spectrometry was used to continuously measure systemic oxygen consumption (VO_2) in 22 infants for 72 hours postoperatively. Arterial, superior vena caval and pulmonary venous blood gases were measured at 2 to 4 hour intervals to calculate CO. The comprehensive Aristotle score was collected.

Hospital mortality was 4.5%. The comprehensive Aristotle score ranged from 14.5 to 23.5 and negatively correlated with CO ($P = 0.027$). Among the patient-adjusted factors, myocardial dysfunction ($n = 10$), mechanical ventilation to treat cardiorespiratory failure ($n = 9$) and atrioventricular valve regurgitation ($n = 4$) ($P = 0.01$) negatively correlated with CO ($P = 0.06$ to 0.07). Aortic atresia ($n = 9$) was associated with a lower CO ($P = 0.01$) for the first 24 hours which linearly increased overtime ($P = 0.0001$). No correlation was found between CO and other factors ($P > 0.3$ for all).

Conclusions: Comprehensive Aristotle score significantly negatively correlates with CO after the Norwood procedure. A preoperative estimation of the comprehensive Aristotle score, particularly in association with myocardial dysfunction, mechanical ventilation to treat cardiorespiratory failure, atrioventricular valve regurgitation and aortic atresia may help to anticipate a high postoperative morbidity with low cardiac output syndrome.

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The Aristotle score has been developed as a new concept of a precise and quantitative measurement of complexity in congenital heart surgery.^{1,2} It consists of two parts: the basic score, a procedure-adjusted complexity score that is based on the potential for mortality, potential for morbidity, and anticipated technical difficulty; and the comprehensive score, a complexity score adjusted according to specific patient characteristics, including procedure-dependent factors (anatomic variations and associated procedures) and procedure-independent factors (clinical status of the patient). Although still undergoing validation, the Aristotle score is emerging as a useful tool to evaluate surgical results.³⁻⁶

The Norwood procedure has a basic score 14.5, the second highest among 145 currently scored procedures. The Norwood procedure also has a large dispersion of case complexity because of a wide spectrum of cardiac and noncardiac lesions,^{7,8} with as many as 10 additional points in the comprehensive score (Table 1). A significant correlation has been reported between the comprehensive Aristotle score and early and late postoperative mortality after the Norwood procedure.^{3,4} Early postoperative mortality remains about 10% to 25%, largely resulting from myocardial dysfunction and low cardiac output (CO).^{3,4,9} Indeed, as we have recently shown, early

Abbreviations and Acronyms

CO	= cardiac output
Do ₂	= oxygen delivery
ERo ₂	= oxygen extraction ratio
Q _p	= pulmonary perfusion
Q _s	= systemic perfusion
VO ₂	= systemic oxygen consumption

post-Norwood course is characterized by profound hemodynamic instability and impaired balance of oxygen transport.¹⁰ In this study, we therefore sought to determine the correlations between the comprehensive Aristotle score, analyzing each of the patient-adjusted complexity factors, and CO and oxygen transport variables during the early postoperative period after the Norwood procedure.

Materials and Methods**Patients**

This study was approved by the research ethics board at the Hospital for Sick Children, Toronto, Ontario, Canada. Written, informed consent was obtained from the parents of 22 patients (18 of them boys, age range 4–92 days, median age 7 days) undergoing a classic Norwood procedure with modified Blalock–Taussig shunt between February 2004 and February 2007. During the same period, an additional 10 patients who also underwent the Norwood procedure with modified Blalock–Taussig shunt were not offered study participation because of equipment or technical support availability. Patients undergoing the modified Norwood procedure with a right ventricle–pulmonary artery conduit or a hybrid procedure (bilateral pulmonary arterial banding and arterial duct stenting) during this period were excluded from the study to avoid the confounding effects of operative techniques on total CO. The clinical characteristics of the patients are shown in Table 2.

Surgical Techniques

All patients were intubated with cuffed endotracheal tubes (Microcuff-Heidelberg-Pediatric; Microcuff GmbH, Weinheim, Germany). The neo-aortic reconstruction was performed with cardiopulmonary bypass (131 ± 33 minutes) and moderate to deep hypothermia (18°C–25°C). Selective cerebral perfusion was used in all 22 patients (46 ± 23 minutes), associated with a short period of circulatory arrest (14 ± 14 minutes).¹¹ The 3.5-mm right modified Blalock–Taussig shunt was then completed with anastomosis of the distal conduit to the central pulmonary artery. All patients received methylprednisolone (30 mg/kg) before cardiopulmonary bypass. Phenoxybenzamine (0.25 mg/kg) was given at initiation of cardiopulmonary bypass. Milrinone (0.66 µg/[kg %2219 min]) and dopamine (5 µg/[kg · min]) were administered at the time of cessation of cardiopulmonary bypass. Modified ultrafiltration was performed in all cases. Pulmonary venous and superior vena caval lines were inserted.

Postoperative Management

The central (esophageal) temperature was maintained between 36°C and 37°C. Postoperative monitoring included arterial, superior vena caval, and pulmonary venous pressures; heart rate; and end-tidal

TABLE 1. Aristotle scores for the Norwood procedure

Basic score	14.5
Procedure-dependent factors	
Aortic atresia	3
Obstructed atrial septal defect	4
Atrioventricular regurgitation	3.5
Total anomalous pulmonary venous connection repair	4
Age >1 mo	3
Procedure-independent factors	
Mechanical ventilation to treat cardiorespiratory failure	2
Myocardial dysfunction	2

carbon dioxide. Sedation consisted of continuous intravenous infusion of morphine and intermittent injections of a muscle relaxant (pancuronium) and lorazepam as required. Patients received time-cycled pressure-control/pressure-support ventilation. Ventilation volume and rate were adjusted to control arterial PCO₂. Arterial oxygen saturation was maintained between 70% and 85%. Hemoglobin was maintained between 14 and 16 mg/dL. Vasoactive drugs (milrinone, phenoxybenzamine, and vasopressin) and volume infusions (5% albumin or blood) were administered according to our standard protocol.¹²

Measurements of CO, Oxygen Delivery, and Oxygen Extraction Ratio

Systemic oxygen consumption ($\dot{V}O_2$) was measured continuously with an AMIS2000 mass spectrometer (Innovision A/S, Odense, Denmark) during the first 72 hours after arrival in the cardiac intensive care unit.¹³ In combination with aortic, superior vena caval, and pulmonary venous blood gas measurements, pulmonary blood flow ($\dot{Q}_p$) and systemic blood flow ($\dot{Q}_s$) were then calculated with the direct Fick method. Total CO is the sum of $\dot{Q}_p$ and $\dot{Q}_s$. Oxygen delivery (Do₂) is equal to the product of $\dot{Q}_s$ and arterial oxygen content. Oxygen extraction ratio (ERo₂) is the ratio $\dot{V}O_2$ to Do₂. These values were collected at 2-hour intervals during the first 24 hours and at 4-hour intervals in hours 25 through 72.

Calculation of Comprehensive Aristotle Scores

Preoperative data for calculation of comprehensive Aristotle scores were collected retrospectively. The comprehensive Aristotle score was calculated according to the scoring system published by the Aristotle committee in 2004 (Aristotle Institute, Denver, Colo; <http://www.aristotleinstitute.org>). The most frequent procedure-dependent and procedure-independent factors in the series are shown in Table 1.

Data Analysis

Data are expressed as mean ± SD. Mixed linear regression for repeated measures was used to analyze the correlations between $\dot{Q}_p$, $\dot{Q}_s$, CO, and oxygen transport variables and the comprehensive Aristotle scores, each of the accounted individual patient-adjusted risk factors, demographic data (age, weight, and body surface area), and intraoperative demographic characteristics (durations of cardiopulmonary bypass, aortic crossclamping, and total circulatory arrest). The extent of correlation was indicated by parameter estimate and *P* values. The comparisons of the values of $\dot{Q}_p$, $\dot{Q}_s$, and

TABLE 2. Demographic data, the patient-adjusted factors and comprehensive Aristotle score in the 22 patients undergoing the Norwood procedure

Patient	Age (d)	Weight (kg)	BSA (m ²)	Diagnosis	Patient-adjusted factors	Aristotle score
1	55	3.8	0.24	DORV, VSD, hypoplastic aortic and mitral valves	RV dysfunction, aberrant right subclavian artery	18.5
2	9	3.6	0.24	HLHS, AA, MS	AA	17.5
3	7	3.5	0.23	HLHS, AS, MS, endocardial fibroelastosis of LV	RV and LV dysfunction, AV regurgitation, mechanical ventilation	22
4	4	3.7	0.25	HLHS, AS, MS, TAPVC	RV dysfunction, TAPVC repair, mechanical ventilation	22.5
5	7	4.0	0.26	HLHS, AA, MS	AA, RV dysfunction, AV regurgitation	22
6	16	3.5	0.24	HLHS, AS, MS, endocardial fibroelastosis of LV	RV and LV dysfunction, mechanical ventilation	19.5
7	7	4.2	0.27	HLHS, AA, MA	AA, RV dysfunction, mechanical ventilation	21.5
8	12	3.5	0.23	DILV, TGA, VSD	LV dysfunction, mechanical ventilation	18.5
9	6	3.5	0.23	HLHS, AA, MA	AA, AV regurgitation	19.5
10	92	4.1	0.26	DILV, TGA, ASD, VSD	Age >1 mo	17.5
11	16	3.9	0.25	HLHS, AS, MS	RV dysfunction, obstructive ASD, AV regurgitation, mechanical ventilation	23.5
12	7	4.0	0.25	HLHS, AS, MS		14.5
13	6	2.9	0.2	HLHS, AS, MS	RV dysfunction, mechanical ventilation	18.5
14	7	2.8	0.19	HLHS, AA, MS	AA	17.5
15	7	3.6	0.24	Crisscross heart, VSDs, hypoplastic aortic arch	Crisscross heart, dextrocardia	15.5
16	5	2.5	0.18	HLHS, AS, MA		14.5
17	4	4.2	0.27	HLHS, AS, MA, TAPVC	TAPVC repair	18.5
18	5	3.9	0.26	HLHS, AA, MA	AA	17.5
19	4	3.1	0.21	HLHS, AA, MS	AA, RV dysfunction, mechanical ventilation	21.5
20	7	3.2	0.21	TA, TGA, hypoplastic aortic arch		14.5
21	10	3.4	0.24	HLHS, AA, MS	AA, obstructive ASD	19.5
22	4	3.6	0.23	HLHS, AA, MA	AA	17.5

BSA, Body surface area; DORV, double-outlet right ventricle; VSD, ventricular septal defect; RV, right ventricle; HLHS, hypoplastic left heart syndrome; AA, aortic atresia; MS, mitral stenosis; LV, left ventricle; AV, atrioventricular; TAPVC, total anomalous pulmonary venous connection; MA, mitral atresia; DILV, double-inlet left ventricle; TGA, transposition of great arteries; ASD, atrial septal defect; AS, aortic stenosis; TA, tricuspid atresia.

CO between patients with a comprehensive Aristotle score >20 and those with a score ≤20 were made by unpaired *t* test. All data analysis was performed with SAS statistical software version 9.2 (SAS Institute, Inc, Cary, NC).

Results

Patients

Among the 22 patients enrolled in the study, there were no episodes of circulatory collapse and no heart transplants during the hospital stay. One patient died of cardiac failure on postoperative day 25 (patient 19), and the in-hospital mortality (also 30-day mortality) was thus 4.5% (1/22 patients). Patients were extubated between 4 to 90 days (median 10 days) and stayed in the hospital for 15 to 270 days (median 24 days). Among the additional 10 patients who were not enrolled in this study, there were no deaths.

Comprehensive Aristotle Score

Table 2 shows the patient-adjusted factors and comprehensive Aristotle scores for the 22 patients. The comprehensive

Aristotle score ranged from 14.5 to 23.5 (mean 18.6 ± 2.7 , median 18.5). The score was greater than 20 for 27% of patients (6/22). The most frequent patient-adjusted factors were myocardial dysfunction (*n* = 10), mechanical ventilation to treat cardiorespiratory failure (*n* = 9), aortic atresia (*n* = 9), and moderate atrioventricular regurgitation (*n* = 4). The incidences of the patient-adjusted factors are shown in Table 3.

Correlations of CO, $\dot{V}O_2$, Do_2 , and ERo_2 with Comprehensive Aristotle Score, Individual Patient-Adjusted Factors, and Clinical Demographic Data

CO was significantly and negatively correlated with the comprehensive Aristotle score (*P* = .027; Figure 1). Mean CO was significantly lower in patients with a score greater than 20 than in those with a score less than 20 (3.79 ± 0.98 and 4.80 ± 1.36 L/min per m², respectively, *P* < .0001). Further analysis of each of the individual patient-adjusted factors showed a trend toward lower CO in

TABLE 3. Correlations of the comprehensive Aristotle score, individual patient-adjusted factors, and clinical demographic data with total cardiac output

Variable	Intercept	Parameter estimate	P value
Aristotle score	7.92	−0.18	.03
Procedure-dependent factors			
Aortic atresia (n = 9)	4.77	−0.58	.21
Aortic atresia	4.75	−1.20	0.01
Aortic atresia × time		0.022	< 0.0001
Obstructed ASD (n = 2)	4.54	−0.17	.83
AV regurgitation (n = 9)	4.72	−0.10	.07
TAPVC repair (n = 2)	4.47	0.64	.43
Age >1 mo	4.48	0.004	.75
Procedure-independent factors			
Mechanical ventilation to treat cardiorespiratory failure (n = 9)	4.86	−0.82	.07
Myocardial dysfunction (n = 10)	4.9	−0.83	.06
Clinical demographic data			
Weight (kg)	5.26	0.20	.69
Body surface area (m ²)	4.97	0.19	.94
Duration of CPB (min)	3.77	0.006	.42
Duration of ACC (min)	3.65	0.010	.21
Duration of circulatory arrest (min)	4.28	0.017	.30

For the procedure-dependent and procedure-independent factors, the intercept indicates the mean value of total cardiac output in patients without this factor, whereas the parameter estimate indicates the difference in total cardiac output between patients with the factor and those without the factor. ASD, Atrial septal defect; AV, atrioventricular; TAPVC, total anomalous pulmonary venous connection; CPB, cardiopulmonary bypass; ACC, aortic crossclamping.

patients with preoperative myocardial dysfunction ($P = .064$), mechanical ventilation to treat cardiorespiratory failure ($P = .068$), and atrioventricular regurgitation ($r = 0.069$). Aortic atresia was not significantly correlated with overall CO levels ($P = 0.21$). But aortic atresia was associated with a lower CO ($P = 0.01$) for the first 24 hours which linearly increased overtime ($P = 0.0001$); a trend not observed with the other complexity factors ($P = 1.0$). There was no significant correlation between CO and the presence of..., obstructed atrial septal defect, repair of total anomalous pulmonary venous connection, age older than 1 month, or any other factors ($P > .2$ for all). CO was not correlated with weight, body surface area, or the durations of cardiopulmonary bypass, aortic crossclamping, and circulatory arrest ($P > .2$ for all). Furthermore, there was no significant correlation between the comprehensive Aristotle score and oxygen transport variables ($P = .17$ for Do_2 and ERo_2 and $P = .7$ for $\dot{\text{V}}\text{O}_2$) or with the duration of either mechanical ventilation or hospital stay.

Discussion

The Aristotle score was developed on the basis of the opinions of expert surgeons from many countries.¹ Although

Figure 1. Correlation of repeatedly measured total cardiac output and comprehensive Aristotle score in 22 patients in first 72 hours after Norwood procedure.

the Aristotle score is under a validation process and will be soon based on real harvested data,^{1,14,15} our data provide partial support for its potential utility in decision making and outcome prediction. In this study, the comprehensive Aristotle score was negatively correlated with postoperative CO after the Norwood procedure, but it was not correlated with the “hard” clinical end points of death, duration of ventilation, or hospital stay in this small cohort. In light of the relatively small number of patients studied, failure to demonstrate a relationship between the comprehensive Aristotle score and mortality and morbidity was unsurprising; however, our demonstration of the relationship between the comprehensive Aristotle score (and some important individual determinants) and detailed assessment of postoperative physiology could shed light on the mechanisms of increased mortality and morbidity seen in other studies.^{3,4}

Clearly, we could not relate the comprehensive Aristotle score to mortality in our series.^{16,17} Similarly, this study was not sufficiently powered to show a relationship with other clinical end points, such as duration of mechanical ventilation and hospital stay. Our study focused on CO because it is one of the most important determinants of the postoperative morbidity and mortality after the Norwood procedure.^{9,18} Our data did demonstrate a significant negative correlation between the comprehensive Aristotle score and repeatedly measured CO during the first 72 hours after the Norwood procedure. It has been shown that patients with a score greater than 20 have significantly higher morbidity and mortality after the Norwood procedure.^{3,4} Our data showed that mean CO was significantly lower in patients with a score greater than 20 than in those with a score less than 20. In absolute terms, this amounted to a difference of approximately 1 L/(min · m²). Our study further identified trends toward significant effects on postoperative CO of procedure-independent factors,

including myocardial dysfunction, mechanical ventilation to treat cardiorespiratory failure, and atrioventricular regurgitation; Interestingly, the presence of an aortic atresia seemed to be associated with a reduced CO for the first 24 hours. This observation might be in relation with a temporary decreased coronary blood flow in patients with aortic atresia. These trends did not exist for the presence of age at operation, and intraoperative demographic data, factors that have previously been identified as important complexity factors for perioperative outcome.^{3,15,19,20} It should be mentioned that although some of the factors trended toward statistical significance, the comprehensive Aristotle score (the collective complexity score) was what increased the sensitivity and was significantly correlated with postoperative CO. We also analyzed the correlations with oxygen transport variables but did not find any significant correlations with $\dot{V}O_2$, DO_2 , or ER_{O_2} . This is not entirely surprising, because the three identified important factors (myocardial dysfunction, mechanical ventilation to treat cardiorespiratory failure, and atrioventricular regurgitation) have direct impact on CO, whereas the factors contributing to the variability of $\dot{V}O_2$, DO_2 and ER_{O_2} are more complicated, involving systemic inflammatory response, temperature, arterial oxygen content, and ratio of $\dot{Q}_p$ to $\dot{Q}_s$.^{10,13}

Our findings have several important implications. First, preoperative estimation of the comprehensive Aristotle score may help to anticipate a higher risk of an adverse postoperative course with lower CO in patients after the Norwood procedure. Special consideration should be given to some of the identified important patient-adjusted complexity factors, such as myocardial dysfunction, mechanical ventilation to treat cardiorespiratory failure, and atrioventricular regurgitation as well as aortic atresia. Whether this knowledge can translate to improved outcomes as a result of more aggressive maintenance of optimal myocardial function^{9,21,22} or modification of oxygen demands^{10,23,24} remains to be seen, but such information may allow complexity stratification in the study of such therapies in the future. Secondly, although little can be done to reduce the impact of procedure dependent-factors, except the age at operation, there may be potential for positive influence on procedure-independent factors, such as treatment of myocardial dysfunction, before the Norwood procedure. For example, it has been reported that preoperative use of phenoxymethylamine can help to avoid mechanical ventilation and reduce mortality before the Norwood procedure.¹⁷ Finally, our data on the varied degrees of correlation between the individual complexity factors and CO may provide useful information for refinement of understanding the comprehensive Aristotle score.

Limitations

Only a small number of patients were studied, all the patients had body weights of at least 2.5 kg. Thus, some procedure-dependent and procedure-independent factors that may

potentially affect CO, such as body weight less than 2.5 kg, intact interatrial septum, and repair of total anomalous pulmonary venous connection, thus could not be evaluated.

Conclusions

The comprehensive Aristotle score was significantly and negatively correlated with CO during the early postoperative period after the Norwood procedure. A high preoperative comprehensive Aristotle score (>20), particularly in association with myocardial dysfunction, mechanical ventilation to treat cardiorespiratory failure, and atrioventricular regurgitation as well as aortic atresia may help to anticipate a high postoperative morbidity with low CO syndrome and to promote special strategies to prevent this.

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