Original Article

Aortic Saturation Predicted Operability in Acyanotic Congenital Heart Disease with Left-to-Right Shunt

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Background: Cardiac catheterization is the gold standard to determine operability in patients with congenital heart disease (CHD) with left to right shunt and pulmonary hypertension.

Objective: To determine if systemic oxygen saturation could be used as a screening tool for acyanotic CHD patients who are operable without having to undergo an invasive procedure.

Materials and Methods: All cardiac catheterization data at the King Chulalongkorn Memorial Hospital between 2002 and 2017 were retrospectively reviewed. The inclusion criteria were acyanotic lesion with left-to-right shunt, mean pulmonary artery pressure of 25 mmHg or more, pulmonary overcirculation (Qp:Qs greater than 1), and absence of significant left sided heart disease (LAP or PCWP of less than 15 mmHg). Operability was defined as Rpi of 6 WU.m^2 or less and Rp:Rs of less than 0.3 in room air. The value of aortic saturation as diagnostic test for operability was analyzed by ROC curve analysis.

Results: Two hundred twenty-six patients, with a median age of two years old, (IQR 0.11, 6.00) were divided into pre-tricuspid shunt (ASD, PAPVR, 9.7%), complete atrioventricular (AV) canal defect (13%), and other post-tricuspid lesion (VSD, PDA, 77%). Aortic saturation cut-off values to predict operability with 100% specificity were 98.5% in pre-tricuspid shunt, 100% in post-tricuspid shunt group, and 94.5% in complete AV canal group.

Conclusion: In the present study population, aortic saturation may be used to determine operability in acyanotic CHD patients with pulmonary overcirculation. Diagnostic yield is best in patients with complete AV canal defect in whom oxygen saturation of 95% or above identified operability with close to 100% specificity. In other lesions, there appears to be no oxygen saturation that is safe to preclude cardiac catheterization.

Keywords: Congenital heart disease, Acyanotic heart disease, Non-cyanotic heart lesions, Pulmonary hypertension, Operability, Aortic saturation

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In limited medical resources countries, most congenital heart patients are still late presenters. The treatment choices for congenital acyanotic heart patients with large left to right shunt lesions who already developed pulmonary hypertension are challenging. Currently, there are several criteria that predicts operability in an individual patient with pulmonary hypertension. Most of the criteria is based on calculation from invasive cardiac catheterization. While the availability of pediatric cardiac catheterization suits may be limited in developing countries, blood gas analysis machines are more accessible and can be used to pre-select those patients who may not need cardiac catheterization to determine the operability.

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Background

Approximately 0.8 to 1% of babies are born with congenital heart disease (CHD). Most of these patients have simple defects that lead to systemic to pulmonary shunt such as atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), and atrioventricular canal defect (AVCD). During infancy periods, these patients are well saturated but are suffering from volume overload in pulmonary circulation. The longstanding increase in pulmonary blood flow results in pulmonary vascular structural changes and

increase pulmonary pressure. Nearly all patients with large left-to-right shunt who remain untreated will develop pulmonary arterial hypertension (PAH)[1]. The patients may finally develop pulmonary vascular obstructive disease (PVOD) with gradual decrease in the symptoms of congestive heart failure. At the later stage, shunting across the defect will become right to left and the patient will develop significant desaturation. This condition is called Eisenmenger syndrome. Attempting to close the defect at this stage is associated with high morbidity and mortality[2]. Early detection and appropriate timing of treatment is crucial to avoid unfavorable outcomes.

In developing countries, patients with CHD, especially those who live in rural area, may not seek medical attention due to varieties of reasons. Late presentation and late referral are still major problems in regions with limited resources. The treatment outcomes of patients with moderate to severe PVOD are complicated by postoperative pulmonary hypertensive crises and may increase risk of persistent postoperative PAH[3]. According to the European Society of Cardiology Guideline 2015[4] and the American Heart Association (AHA) Guideline 2015[5], cardiac catheterization is the gold-standard to determine operability in children with CHD and PVOD. Unfortunately, pediatric catheterization suits are not always widely available in developing countries. In the authors' country, with the total population estimated at 70 million people in 2018, only 10 referral centers for congenital heart defects can perform pediatric cardiac catheterization. However, each province has their own local hospital and almost every local hospital can perform blood gas analysis. The authors postulated that systemic oxygen saturation may be helpful to screen the operability of some patients who may be able to undergo heart surgery without having to undergo an invasive cardiac catheterization procedure.

Objective

The present study aimed to determine whether systemic oxygen saturation could be used as a screening tool for patients with acyanotic CHD who are operable without having to undergo cardiac catheterization procedure.

Materials and Methods

Definition and diagnosis

The diagnosis of PAH was made when resting mean pulmonary artery pressure was 25 mmHg or more from cardiac catheterization during spontaneous breathing in room air (Pediatric Pulmonary Hypertension Guidelines, The AHA and the American Thoracic Society (ATS) 2015)[5].

Patients were classified as operable when as pulmonary vascular resistance (PVR) index (Rpi) of 6 Wood Unit.m² or less and PVR-to-systemic vascular resistance (SVR) ratio (Rp:Rs) of less than 0.3, based on AHA and ATS guideline 2015[5].

Study population

The present study was a single hospital-based cases review. Study population derived from all pediatric patients that underwent cardiac catheterization at King Chulalongkorn Memorial Hospital (KCMH) between January 1, 2002 and December 31, 2017. Medical records of the patients were retrospectively reviewed after the approval was received from the Ethic Committee of the Faulty of Medicine, Chulalongkorn University (IRB No.663/60).

The inclusion criteria were as followed:

1. Simple acyanotic lesion with left-to-right shunt (mostly ASD, VSD, PDA and complete AVCD).
2. Mean PA pressure of 25 mmHg or more.
3. Pulmonary overcirculation (Qp:Qs of more than 1).

The exclusion criteria were as followed:

1. Patients with incomplete hemodynamic data.
2. Patients with complex cardiac lesions that exhibited right-to-left shunt as well as left-to-right shunt.
3. Patients with left-sided heart disease, defined by pulmonary arterial wedge pressure (PAWP) or left atrial pressure (LAP) of more than 15mmHg.
4. Patients younger than one month old.

Data collection

Demographic data, cardiac diagnosis, co-morbidity, age at catheterization, echocardiogram findings, hemodynamic data, treatments, and outcomes were collected.

Statistical analysis

The IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA) were used to performed statistical analyses. Continuous data were expressed as median and interquartile range (IQR). The nominal data were expressed as percentage. Receiver operative characteristic (ROC) curve analyses were used to analyze the value of aortic saturation as diagnostic test for operability across 1) all cases and 2) divided by cardiac defects to 2.1) pre-tricuspid shunt (ASD), 2.2) post-tricuspid

Table 1. The clinical characteristics of each subgroups (n=226)

	All; n (%)	Pre-tricuspid shunt; n (%)	Post-tricuspid shunt (except AVCD); n (%)	Complete AVCD; n (%)
No. of subject	226 (100)	22 (9.7)	174 (77.0)	30 (13.3)
Male	93 (41.2)	10 (45.5)	73 (42.0)	10 (33.3)
Down syndrome	42 (18.6)	3 (13.6)	29 (16.7)	10 (33.3)
Patients with inoperable cardiac catheterization data	109 (48.2)	6 (27.3)	87 (50.0)	16 (53.3)

AVCD=atrioventricular canal defect

Table 2. The cardiac catheterization data of each subgroups (n=226)

	All; median (IQR)	Pre-tricuspid shunt; median (IQR)	Post-tricuspid shunt (except AVCD); median (IQR)	Complete AVCD; median (IQR)
Aortic saturation (%)	95.0 (91.0, 97.0)	94.5 (91.0, 97.3)	95.0 (92.8, 97.0)	89.0 (85.8, 92.3)
mPAP (mmHg)	48.0 (34.0, 62.3)	32.5 (27.8, 44.3)	50.0 (34.0, 63.0)	58.5 (38.5, 64.8)
Qp:Qs	1.92 (1.46, 2.63)	2.26 (1.67, 3.66)	1.90 (1.44, 2.42)	2.11 (1.52, 3.21)
PVRi (Wood unit.m^2)	4.02 (2.40, 6.06)	2.16 (1.27, 4.11)	4.11 (2.75, 6.03)	4.64 (2.17, 8.07)
PVR:SVR	0.28 (0.18, 0.43)	0.17 (0.08, 0.29)	0.29 (0.19, 0.43)	0.30 (0.19, 0.59)

AVCD=atrioventricular canal defect; mPAP=mean pulmonary arterial pressure; Qp:Qs=pulmoanry blood flow to systemic blood flow ratio; PVRi=pulmonary vascular resistance index; PVR:SVR=pulmoanry vascular resistance to systemic vascular resistance; IQR=interquartile range

shunt excluding complete atrioventricular (AV) canal, and 2.3) complete AVCD. The patients who had both pre-tricuspid and post-tricuspid shunt, such as ASD and VSD, secundum ASD, and complete AV canal, were included into the post-tricuspid shunt or complete AV canal group.

Results

Clinical characteristic

Four thousand ninety patients underwent cardiac catheterization at KCMH between January 1, 2002 and December 31, 2017. Two hundred twenty-six patients met the inclusion criteria for the present study. The baseline clinical characteristics are shown in Table 1. Forty-one percent of patients were male. Median age at cardiac catheterization date was two years old (IQR 0.11, 6.00). Median pulmonary to systemic blood flow (Qp:Qs) was 1.92 with median PA pressure of 48.0 mmHg. Most patients had post-tricuspid shunt (174 patients, 77%). Twenty-two patients (9.7%) had pre-tricuspid shunt including nine with ASD secundum, eight with ASD primum, three with ASD sinus venosus, and two with common atrium. The other 30 patients (13%) had complete AVCD. The cardiac catheterization data of each subgroups are shown in Table 2.

Aortic saturation cut-off point

The operability was defined as pulmonary resistance index of 6 Wood Unit.m² or less and PVR:SVR ratio of less than 0.3 in room air[5]. ROC plot was used to analyze the cut-off value of aortic saturation as diagnostic test for operability. Saturation of more than cut-off value defined the likelihood of having operable cardiac catheterization data in each patient. The aortic saturation of 94.5% was able to predict the operability of the acyanotic congenital heart patient with the sensitivity of 70.9% and the

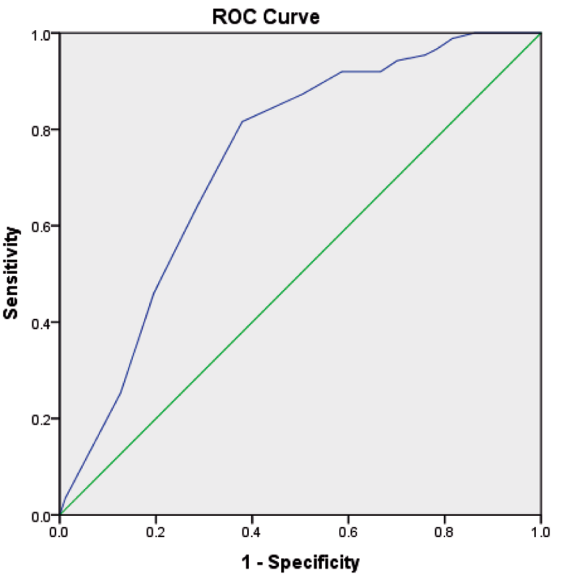

Figure 1. The ROC of cut-off value of aortic saturation as diagnostic test for operability of patients with acynaotic congenital heart disease. The aortic saturation of 94.5% has the highest sensitivity of 70.9% and the specificity of 67.9%.

Table 3. The best cut-off value and the cut-off value with 100% specificity of aortic saturation as diagnostic test for operability of each subgroups

Patients group	AUC	p-value	Aortic sat cut-off value	Sensitivity	Specificity	Aortic sat with 100% specificity (sensitivity)
All	0.725	<0.001	94.5%	70.9%	67.9%	100% (0.0%)
Pre-tricuspid shunt	0.693	0.173	93.0%	75.0%	67.0%	98.5% (6.3%)
Post tricuspid shunt (except complete AVCD)	0.738	<0.001	94.5%	81.6%	62.1%	100% (0.0%)
Complete AVCD	0.77	0.012	89.5%	78.6%	81.3%	94.5% (21.4%)

AUC=area under the ROC curve; AVCD=atrioventricular canal defect

specificity of 67.9% (Figure 1). The aortic saturation values that had the best sensitivity and specificity, and the values with 100% specificity of operability are shown in Table 3.

The data showed that only patients with 98.5% to 100% saturation in room air could undergo corrective surgery safely without undergoing pre-operative catheterization in pre-tricuspid shunt and post-tricuspid shunt groups, with a specificity of 100%. In complete AVCD group, the aortic saturation value that demonstrated the best sensitivity and specificity were 89.5%. However, the oxygen saturation should be 94.5% or above to predict which patients with complete AVCD would be operable with close to 100% specificity.

Discussion

PAH is one of the most important complications in children with CHD. In developed countries, early identification and early treatment had significantly reduced the incidence of PAH. In contrast, the prevalence of PAH associated with CHD is still high in limited resources countries due to difficulty in accessing specialized care and delayed treatment.

Non-cyanotic CHD associated with left-to-right shunt comprises about half of patients with CHD treated in the present study hospital. Many of these patients with significant left-to-right shunt were referred late and already had PAH at presentation. When echocardiogram suggested presence of significant pulmonary hypertension, these patients were usually referred for cardiac catheterization to determine operability. Question often arose if some of these patients without significant oxygen desaturation in room air could undergo cardiac surgery without the need for cardiac catheterization to save cost and potential complications from the procedure. In the present study, the authors sought to determine if there was a safe range of oxygen saturation that can determine operability with close to 100% specificity in patients with acyanotic CHD with left-to-right shunt and evidence of significant PAH.

In the present study, although aortic oxygen saturation can be used to predict operability with relatively good sensitivity and specificity, the only group of patients in whom the oxygen saturation could reasonably be used to predict operability with close to 100% specificity is those affected with complete AV canal. With a cut-off of 94.5%, a patient with complete AV canal could be safely predicted to be operable in patients with ASD or other post-tricuspid shunt, including VSD and PDA, only when oxygen saturation exceeded 98.5 or 100%, respectively. The sensitivity of 6.3 and 0% in ASD and post-tricuspid shunt group at 100% specificity means that relatively few patients can be exempted from cardiac catheterization by using systemic oxygen saturation as a screening tool in these group. On the contrary, approximately one out of five patients with complete AV canal could safely be exempted from cardiac catheterization if systemic oxygen saturation was more than 94.5% in the present study cohort.

The authors postulate the reason of the oxygen saturation could be used in patients with complete AV canal to predict operability, while there was no "safe zone" for oxygen saturation in patients with VSD or PDA, has to do with the characteristic of the shunt in these diseases. Due to a large defect, patients with complete AV canal generally have some right-to-left shunt with significant PAH, while this may not be the case in patients with VSD or PDA. A linear dropping of oxygen saturation with increasing degree of PAH in patients with complete AV canal enable it to be used to predict operability, while in patients with VSD, the degree of PAH has to be extreme for the patient to develop right-to-left shunt. Patients with ASD (pre-tricuspid shunt) appeared to fall in between these former two groups, probably because with increasing PAH, right-to-left shunting via an ASD can also occur earlier than patients with VSD as shunting in ASD depends more on the relative

diastolic compliance of the right and left ventricle and not the direct difference between systolic pressure in the two ventricular chambers.

Limitation

The present study used oxygen saturation determined during cardiac catheterization as the predictor for operability. The authors postulate that systemic oxygen saturation from lower extremity obtained by blood gas could be used in the real clinical setting although this has not been prospectively tested. Physicians should be cautious for using the present study data with trans-cutaneous determination of systemic oxygen saturation as it is probably less accurate with higher variability among different brand of pulse oximeter.

The present study is a single hospital based retrospectively review, some of patients' information were not available. Secondly, most of the population in the present study were post-tricuspid shunt (77%), while complete AVCDs and pre-tricuspid shunt were found in only 13.3%, and 10% respectively. An additional prospective study will be helpful to confirm these findings.

Conclusion

In developing countries, access to specialist health services is limited. Therefore, aortic saturation, obtained by blood gas analysis, of more than 95% may be used to identified operability in patients with complete AV canal. This is not used in other cardiac defects with left to right shunt such as VSD and ASD where there may not be a safe cut-off oxygen saturation to preclude cardiac catheterization.

What is already known on this topic?

Because of the limited medical resources in the authors' country, most of the congenital heart patients are late presenters. The treatment choices for congenital acyanotic heart patients with large left to right shunt lesions who already developed pulmonary hypertension are challenging. Currently, there are several criteria to predict the operability in an individual patient with pulmonary hypertension. Most of the criteria based on calculation from invasive cardiac catheterization. While the availability of pediatric cardiac catheterization suits may be limited in developing countries, blood gas analysis machines are more accessible. Therefore, blood gas analysis machines could be used to pre-select those patients who may not need cardiac catheterization to determine operability. The authors postulated that systemic oxygen saturation may be helpful to screen the operability of some patients.

What this study adds?

In this study, the authors report the diagnostic yield of arterial saturation to determine operability in acyanotic congenital heart patients.

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Conflicts of interest

The authors declare that they have no conflicts of interest with the contents of this article.

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