Oximetry Assessment of Intracardiac and Great Vessel Shunts

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Introduction

Congenital Heart Disease (CHD) affects approximately 8 live births per 1,000 globally, with a higher prevalence in Asia (9.3 per 1,000) and Europe (8.2 per 1,000) vs. a lower incidence in the United States (6.9 per 1,000). Depending on the severity that contributes to overt signs and symptoms, the diagnosis of CHD may occur in utero, after birth, during adolescence or in adulthood. Many defects that are associated with CHD are characterized by a blood flow pattern that deviates from the normal circuit of the adult circulatory system. Patients with this altered blood pathway or shunt may be asymptomatic or present in stages of increasing gravity that severely compromises cardiac output with profound hypoxemia. Included among the most common intracardiac and great vessel shunt lesions are: atrial septal defect, patent ductus arteriosus and ventricular septal defect.

Right-sided cardiac catheterization with the Oximetry Run procedure is a standard assessment technique for the detection, localization and quantification of intracardiac and great vessel left-to-right shunts in all age populations. During the oximetry run, oxygen content (\(c_{\text{tO}_2}\)) and fractional oxyhemoglobin saturation (%\(F_{\text{O}_2}\text{Hb}\)) are measured in blood samples drawn sequentially from the pulmonary artery (PA), right ventricle (RV), right atrium (RA), superior vena cava (SVC), and inferior vena cava (IVC). A left-to-right shunt may be detected and localized if a sudden, discontinuous change or step-up in blood oxygenation is identified in one of the right heart sites assessed. A significant step-up is defined as an increase in blood oxygen content or saturation that exceeds the normal variability that might be observed if multiple samples were drawn from that cardiac chamber or great vessel.

The oximetry run procedure was established by studies that were originally performed by Dexter and his associates in 1947. Oxygen content was measured using Van Slyke and Neil's volumetric technology and pressures were recorded by Hamilton's optical manometer. Their results concluded that repeated specimens drawn from the RA could vary in \(c_{\text{tO}_2}\) by as much as 2 volumes percent (vol%), variation within the RV and PA were found to be 1 vol% and 0.5 vol% respectively. From these observations, Dexter concluded that a significant step-up is present at the atrial level when the highest \(c_{\text{tO}_2}\) in blood samples drawn from the RA exceeds the highest content in the vena cava by 2 vol%， at the ventricular level if the highest RV sample is 1 vol% higher than the highest RA sample, and at the level of the pulmonary artery if the PA \(c_{\text{tO}_2}\) is more than 0.5 vol% greater than the highest RV sample.

The studies performed by Dexter derived the acceptable variability of \(c_{\text{tO}_2}\) in the right heart utilizing a laboratory based analytical method. In 1980, Antman correlated \(c_{\text{tO}_2}\) with oxygen saturation during oximetry run procedures in patients receiving right-heart catheterizations for non-shunt related pathologies. Because of the pioneering work of Dexter and the continued efforts of Antman, point-of-care (POC) whole blood oximetry (hemoximetry), which encompasses multiwavelength spectrophotometry, has replaced volumetric analysis with rapid throughput measurements of \%\(F_{\text{O}_2}\text{Hb}\) and \(c_{\text{tO}_2}\) for step-up shunt detection. Without compromising accuracy or precision, healthcare professionals who are not skilled in the nuances of laboratory technology, can assist in the oximetry run procedure by processing blood specimens and reporting results within 10 seconds. The use of POC whole blood oximetry has simplified the technique and reduced the overall time needed to perform the right-sided cardiac catheterization procedure for step-up shunt detections.

Oximetry Run Procedure

Screening for a left-to-right shunt is commonly performed by measuring the \%\(F_{\text{O}_2}\text{Hb}\) from samples drawn from the SVC and PA. If the difference in \%\(F_{\text{O}_2}\text{Hb}\) between these samples is ≥8%, a left-to-right shunt may be present at the atrial, ventricular, or great vessel level, and a full oximetry run is often conducted.

A full oximetry run to detect a left-to-right shunt typically includes collecting samples from the following anatomic locations and measuring the \%\(F_{\text{O}_2}\text{Hb}\) and \(c_{\text{tO}_2}\):

1. Left and/or right pulmonary artery
2. Main pulmonary artery
3. Right ventricle, outflow tract
4. Right ventricle, mid
5. Right ventricle, tricuspid valve or apex
6. Right atrium, low or near tricuspid valve
7. Right atrium, mid
8. Right atrium, high
9. Superior vena cava, low (near junction with right atrium)
10. Superior vena cava, high (near junction with brachiocephalic vein)
11. Inferior vena cava, high (just at or below diaphragm)
12. Inferior vena cava, low (at L4–L5)

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Table 1: Detection of Left-to-Right Shunts by Oximetry

<table>
<thead>
<tr>
<th>Level of Shunt</th>
<th>Mean of distal chamber samples</th>
<th>Mean of proximal chamber samples</th>
<th>Highest value in proximal chamber</th>
<th>Highest value in distal chamber</th>
<th>Approximate minimal Qp/Qs required for detection (assuming SBFI = 3 L/min/M²)</th>
<th>Possible Causes of Step-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial (SVC/IVC to RA)</td>
<td>≥7</td>
<td>≥1.3</td>
<td>≥11</td>
<td>≥2.0</td>
<td>1.5–1.9</td>
<td>Atrial septal defect; Partial anomalous pulmonary venous drainage; ruptured sinus of Valsalva; VSD with TR; coronary fistula to RA</td>
</tr>
<tr>
<td>Ventricular (RA to RV)</td>
<td>≥5</td>
<td>≥1.0</td>
<td>≥10</td>
<td>≥1.7</td>
<td>1.3–1.5</td>
<td>VSD; PDA with PR; primum ASD; coronary fistula to RV</td>
</tr>
<tr>
<td>Great Vessel (RV to PA)</td>
<td>≥5</td>
<td>≥1.0</td>
<td>≥5</td>
<td>≥1.0</td>
<td>≥1.3</td>
<td>PDA; aortopulmonic window, aberrant coronary artery origin</td>
</tr>
<tr>
<td>Any level (SVC to PA)</td>
<td>≥7</td>
<td>≥1.3</td>
<td>≥8</td>
<td>≥1.5</td>
<td>≥1.5</td>
<td>All of the above</td>
</tr>
</tbody>
</table>

SVC and IVC, superior and inferior vena cava; RA, right atrium; RV, right ventricle; PA, pulmonary artery; VSD, ventricular septal defect; TR, tricuspid regurgitation; PDA, patent ductus arteriosus; PR, pulmonic regurgitation; ASD, atrial septal defect; SBFI, systemic blood flow index; Qp/Qs, pulmonary to systemic flow ratio.

Interpretation of the oximetry run and step-up differences relative to left-to-right shunts, are often modeled on the guidelines published by Grossman, whereby criteria developed by Antman compared both the mean %FO₂Hb of the distal chambers and the highest %FO₂Hb in the proximal chambers for significant step-up findings (Table 1).²

To determine a right-to-left shunt, blood specimens need to be sampled from the left heart, i.e., pulmonary vein, left atrium, left ventricle, and aorta. The pulmonary venous blood of patients with arterial hypoxemia caused by an intracardiac right-to-left shunt is fully saturated with oxygen. Therefore, the site of a right-to-left shunt may be localized by noting which left heart site is the first to show desaturation (i.e., a step-down in oxygen concentration). If the left atrial %FO₂Hb is normal but desaturation is present in the left ventricle and in the systemic circulation, the right-to-left shunt is across a ventricular septal defect. A major disadvantage of this technique is that a pulmonary vein and the left atrium must be entered. This is not as easy in adults as it is in infants, where access to the left atrium may be entered through the foramen ovale.

If the oximetry run reveals that a significant step-up is present, the pulmonary blood flow (Qp), systemic blood flow (Qs), and magnitude of left-to-right or right-to-left shunts may be calculated based on the Fick equation.⁶

**Oximetry and Oxyhemoglobin Saturation**

Many POC devices report oxyhemoglobin saturation. Blood gas analyzers calculate this value using an algorithm based on an assumed normal oxyhemoglobin dissociation curve, PO₂, pH and a preset total hemoglobin value.⁷ Some whole blood oximeters use two light emitting diode wavelengths that have the capacity to only measure the hemoglobin species of oxyhemoglobin (%O₂Hb) and reduced hemoglobin (%HHb).⁸ These systems, which either do not measure hemoglobin directly, or do not detect the full spectrum of hemoglobin species, report functional oxyhemoglobin saturation (SO₂). Because they do not account for concentrations of carboxyhemoglobin (%COHb) or methemoglobin (%MetHb), they inherently report oxygen saturation results with a positive bias when correlated to the laboratory’s gold standard (CO-oximetry).⁹ In the presence of clinically elevated %COHb and %MetHb, patient management based on functional oxygen saturation may contribute to an erroneous assessment of cardiopulmonary function and the inappropriate interpretation of the step-up calculation.¹⁰

Multiwavelength spectrophotometry integrated into POC whole blood oximetry or CO-oximetry is designed to report accurate and precise results of both cto₂ and oxygen saturation.¹¹ These analyzers directly measure %O₂Hb, %HHb, %COHb and %MetHb. The oxygen saturation value reported, which is derived from measuring all the species of hemoglobin, is termed fractional oxyhemoglobin saturation. The total hemoglobin reported is the sum of the concentrations of each hemoglobin derivative in units of g/dL, g/L or mmol/L. Some POC oximetry systems¹² contain software to tag the result with the anatomic location of the sample, calculate the magnitude of the step-up, and perform hemodynamic computations required in the right-side catheterization procedure including:

- Body surface area
- Oxygen uptake
- Stroke volume and stroke index
- Cardiac output
- Pulmonary and systemic blood flow
- Pulmonary and systemic vascular resistance
- Pulmonary-to-systemic blood flow ratio

To promote blood conservation and reduce the risk of iatrogenic anemia especially in the newborn/pediatric population, oximeters and CO-oximeters used in the oximetry run procedure should perform as intended with an instrument sample volume of ≤50 µL.¹³ In addition; the analysis throughput time should be fast enough to accommodate a specimen that is free from
Micro sample specimens that contain even the smallest coating of a liquid anticoagulant can promote hemodilution type preanalytical errors to all results.\textsuperscript{14} Another advantage of the throughput time is the effect to the overall length of the catheterization procedure. Having a time to result in 60 seconds, compared with less than 10 seconds, can disrupt the oximetry run flow by either delaying moving the catheter to the next anatomic location while waiting for the result, or repositioning the catheter to a previous site to resample due to analyzer malfunction or to confirm a past result. These two system design features, small sample volume and time to result, are essential considerations for choosing an optimal analyzer for right-sided catheterization procedures.

The Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS, and National Committee for Clinical Laboratory Standards) cautions the use of functional oxygen saturation measurements (%\textit{FO}_2Hb). Specifically directed at the oximetry run procedure and its associated physiologic calculations, the CLSI guideline states, “Clinically significant errors can result from incorporation of such an estimated value for oxygen saturation in further calculations, such as shunt fraction, or by assuming that the value obtained is equivalent to fractional oxyhemoglobin.”\textsuperscript{16} This identical warning is also published in the Operation Manual of blood gas analyzers and the oximeters that report functional oxyhemoglobin saturation.\textsuperscript{7, 8}

**Summary**

The oximetry run with a step-up or step-down assessment is an established diagnostic procedure in CHD, and is effective in detecting, localizing and quantifying left-to-right and right-to-left intracardiac and great vessel shunts. A contributing factor to ensure accuracy and efficacy in the technique is the selection of the oximetry analyzer. The ideal instrument should: a) report both %\textit{FO}_2Hb and c\textit{tO}_2 results, b) have rapid throughput of samples to minimize overall catheterization time, c) require a small sample volume to promote blood conservation, d) have simple instrument operational characteristics to perform tests proficiently by non-laboratory healthcare professionals, e) tag the result with the anatomic location of the sample, and f) have a low per test cost due to the multiple samples required for each oximetry run procedure. The clinical staff conducting the oximetry run procedure should be familiar with the differences between functional vs. fractional oxygen saturation to avoid potential pitfalls in step-up interpretation and ensure accuracy and consistency in the evaluation of intracardiac and great vessel shunts.

**References**

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12. Avoximeter® 1000E. Accriva Diagnostics Inc. San Diego, CA, USA.