Noninvasive Cardiac Output Estimation by Inert Gas Rebreathing in Mechanically Ventilated Pediatric Patients

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Objective To assess the feasibility and accuracy of inert gas rebreathing (IGR) pulmonary blood flow (Qp) estimation in mechanically ventilated pediatric patients, potentially providing real-time noninvasive estimates of cardiac output.

Study design In mechanically ventilated patients in the pediatric catheterization laboratory, we compared IGR Qp with Qp estimates based upon the Fick equation using measured oxygen consumption (VO_2) ($Fick_{True}$); for context, we compared $Fick_{True}$ with a standard clinical short-cut, replacing measured with assumed VO_2 in the Fick equation ($Fick_{LaFarge}$, $Fick_{Lundell}$, $Fick_{Seckeler}$). IGR Qp and breath-by-breath VO_2 were measured using the Innocor device. Sampled pulmonary arterial and venous saturations and hemoglobin concentration were used for Fick calculations. Qp estimates were compared using Bland-Altman agreement and Spearman correlation.

Results The final analysis included 18 patients aged 4-23 years with weight >15 kg. Compared with the reference $Fick_{True}$, IGR Qp estimates correlated best and had the least systematic bias and narrowest 95% limits of agreement (results presented as mean bias ±95% limits of agreement): IGR −0.2 ± 1.1 L/min, r = 0.90; $Fick_{LaFarge}$ +0.7 ± 2.2 L/min, r = 0.80; $Fick_{Lundell}$ +1.6 ± 2.9 L/min, r = 0.83; $Fick_{Seckeler}$ +0.8 ± 2.5 L/min, r = 0.83.

Conclusions IGR estimation of Qp is feasible in mechanically ventilated patients weighing >15 kg, and agreement with $Fick_{True}$ Qp estimates is better for IGR than for other Fick Qp estimates commonly used in pediatric catheterization. IGR is an attractive option for bedside monitoring of Qp in mechanically ventilated children. *(J Pediatr 2016;177:184-90).*

Serial measurements of cardiac output or pulmonary blood flow (Qp) facilitate optimal management of critically ill children. Unfortunately, reliable bedside measurements of these variables are not readily available, and clinicians frequently rely upon subjective assessments despite poor agreement with objective measurements.[1]

Inert gas rebreathing (IGR) is an established noninvasive technique to estimate Qp and, in the absence of significant intrapulmonary or intracardiac shunting, systemic cardiac output as well. The latest iterations of IGR technology use 0.5% nitrous oxide (N_2O) as the soluble indicator gas and photoacoustic spectroscopy (PAS) for gas analysis, and are able to nontoxically estimate Qp at the bedside in under a minute. IGR reliably estimates Qp in adults,[2-8] and recently, we demonstrated that IGR reliably estimates Qp in children with no intracardiac shunt or pure right-to-left shunt.[9] However, the studied PAS-based device is designed for spontaneously breathing patients and cannot be directly employed in critically ill, mechanically ventilated patients. A ventilator adaptor assembled from standard medical equipment (anesthesia bag, connectors, and pneumatic valves) is available for insertion between the ventilator circuit and endotracheal tube (ETT) to address this issue, but to date, no study has validated the use of the PAS-based device in this population.

The primary aim of this study was to assess the feasibility and accuracy of IGR in mechanically ventilated pediatric patients using the PAS-based device. IGR Qp estimates were compared with reference Qp estimates obtained on the basis of the Fick principle in patients undergoing clinically indicated cardiac catheterization. Given the critical importance of oxygen consumption (VO_2) in the Fick equation and the well-described inaccuracies of VO_2 estimated by published equations,[10-12] we determined Fick Qp using measured VO_2 ($Fick_{True}$) as the reference test. To provide context for the comparison of IGR and $Fick_{True}$ Qp estimates, we also

ETT	Endotracheal tube	N_2O	Nitrous oxide
$Fick_{LaFarge}$	Fick using LaFarge-based VO_2	PAS	Photoacoustic spectroscopy
$Fick_{Lundell}$	Fick using Lundell-based VO_2	Qp	Pulmonary blood flow
$Fick_{Seckeler}$	Fick using Seckeler-based VO_2	Qs	Systemic blood flow
$Fick_{True}$	Fick using measured VO_2	SF_6	Sulfur hexafluoride
IGR	Inert gas rebreathing	VO_2	Oxygen consumption

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compared Fick Qp using equation-based VO_2 values with $Fick_{True}$ Qp because these alternative Fick Qp estimates are commonly employed in pediatric catheterization. Finally, we performed comparisons between VO_2 values that were directly measured, equation-based, and reverse-calculated from the Fick equation (using measured oxygen saturations, hemoglobin concentration, and IGR Qp).

Methods

Patients weighing >9 kg who were scheduled for clinically indicated cardiac catheterization with endotracheal intubation and mechanical ventilation were recruited for the study between September 2014 and March 2015. The weight threshold was chosen based upon theoretical concerns about dead space proportions and gas sampling rate. Patient-related exclusion criteria included left-to-right shunt (based on our previous work demonstrating the unreliability of IGR in this group[9]) or moment-to-moment instability during IGR or saturation measurements. Catheterization-related exclusion criteria included missing data or implausible saturation data, defined as mixed venous or pulmonary artery saturation >85%. IGR-related exclusion criteria included use of N_2O (the soluble test gas) for induction of anesthesia or presence of air leak around the cuffed ETT. Written informed consent to participate in the study was provided by all patients or legal guardians, and the study protocol was approved by the Boston Children's Hospital Institutional Review Board.

Hemoglobin was measured from a peripheral blood sample prior to catheterization. Anesthetic induction and endotracheal intubation were performed and mechanical ventilation initiated by a pediatric cardiac anesthesiologist per routine practice. After intubation with a cuffed ETT and stabilization in 21% oxygen (air), the IGR ventilator adaptor was inserted between the ETT and ventilator, and breath-by-breath VO_2 and IGR Qp were measured using the PAS device as described below. After completion of the PAS measurements, the adaptor was removed from the ventilator circuit. The process was completed either during sterile preparation of the patient or while vascular access was obtained, with the complete protocol typically requiring less than 10 minutes (3-5 minutes for VO_2, 1 minute for IGR), and the catheterization continued without interruption. Clinical and physiologic data were collected on each participant.

PAS Device Configuration

The PAS-based Innocor device and MiniValve ventilator adaptor (both Innovision, Odense, Denmark) were used to measure VO_2 and Qp as shown in **Figure 1**. The MiniValve adaptor inserts between the ventilator and ETT and is composed of a filter (Hygroboy; Nellcor-Covidien, Boulder, Colorado), a pneumotach (Hans Rudolph 4700B, Shawnee, Kansas), 3 pneumatic valves, and an anesthesia bag. The baseline valve configuration of the adaptor allows the patient to be ventilated by the mechanical ventilator (**Figure 1**, A); 51.6 mL of dead space is added to the ventilator circuit. When the rebreathing program is activated, the anesthesia bag fills with the predefined test gas mixture and the valve configuration adjusts

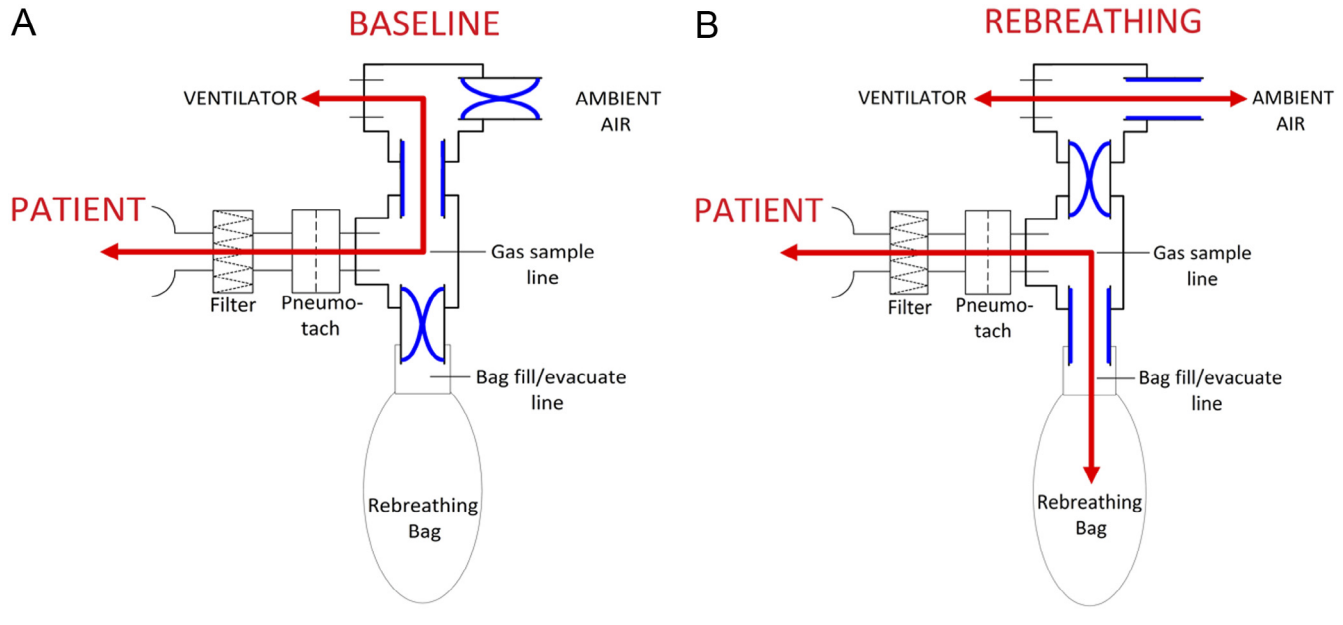

Figure 1. **A,** MiniValve adaptor baseline configuration. The patient's ETT communicates with the ventilator; the filter, pneumotach, and gas sample line are interposed. **B,** Rebreathing configuration. The patient's ETT communicates with the rebreathing bag with the filter, pneumotach, and gas sample line interposed; the ventilator communicates with the room's air. Modified and reprinted with permission from Innovision.