Tissue Hemoglobin Monitoring Is Unable to Follow Variations of Arterial Hemoglobin During Transitions From Pulsatile to Constant Flow in Cardiac Surgery

Olivier Desebbe, MD,*† Cecile Faulcon, MD,* Roland Henaine, MD,‡ Levina Tran, MD,§ Catherine Koffel, MD,* Bertrand Delannoy, MD,* Jean-Jacques Lehot, MD, PhD,|| Olivier Bastien, MD, PhD,*† and Delphine Maucort-Boulch, MD, PhD¶

Objective: **To test whether the variations of tissue hemoglobin concentration (Δ_THb) measured by the FORE-SIGHT™ cerebral oximeter can accurately detect changes in arterial hemoglobin concentration (Δ_AHb) before, during, and after cardiopulmonary bypass.**

Design: **A prospective clinical study.**

Setting: **Cardiac surgery operating room.**

Participants: **Thirty patients scheduled for cardiac surgery.**

Interventions: **Tissue hemoglobin concentration ($_T$Hb) was recorded continuously via 2 sensors applied on the forehead and connected to the cerebral oximeter. Arterial hemoglobin concentration ($_A$Hb) was measured in a hematology analyzer laboratory. Hemodynamic and respiratory parameters as well as epidemiologic data also were noted. Data were collected at 3 perioperative times: After induction of anesthesia, 10 minutes after cardioplegia, and at the end of the surgery.**

Measurements and Main Results: **Ninety pairs of data were collected. The coefficient of linear regression between Δ_THb and Δ_AHb was 0.4 ($p < 0.001$). After exclusion of Hb variations <5%, the trending ability of $_T$Hb to predict Δ_AHb was 87%. However, the Bland and Altman plot graph for $_T$Hb and $_A$Hb showed major limits of agreement (2.4 times the standard deviation). Central venous pressure and carbon dioxide tension were linked independently and positively with $_T$Hb ($p = 0.03$).**

Conclusions: **Continuous monitoring of $_T$Hb cannot accurately track variations of $_A$Hb during the transition from pulsatile to continuous flow and vice versa in cardiac surgery. Local hemodynamic factors such as $PaCO_2$ and vasodilation significantly impact $_T$Hb. In this setting, $_T$Hb monitoring should not be used to guide eventual blood transfusion management.**

KEY WORDS: near-infrared spectroscopy, monitoring, intraoperative, hemoglobin, cardiac surgery, tissue hemoglobin concentration

CONTINUOUS MONITORING OF HEMOGLOBIN concentration could improve transfusion management by detecting acute anemia early as perioperative bleeding is a frequent complication during cardiac surgery.[1,2] It could also reduce unnecessary transfusions,[3,4] which have been proven to increase morbidity, mortality, and healthcare costs.[5–7] Although some devices display continuous measurements of arterial hemoglobin concentration ($_A$Hb),[8–13] accurate $_A$Hb measurement still is obtained through blood draws, which are invasive, time-consuming, and provide discontinuous results.[14] Recently, noninvasive continuous technologies of spectrophotometry-based tissue hemoglobin concentration ($_T$Hb) have been developed to provide immediate clinical information.[15] Moreover, $_T$Hb measurement can be monitored during a pulsatile or a continuous flow state and, therefore, could be useful during cardiac surgery or in patients with artificial hearts in the ICU setting.

Correlation between $_T$Hb and $_A$Hb[15,16–18] is debated due to various determinants of $_T$Hb such as hemodynamic local factors.[15] However, if variations of $_T$Hb correlated with variations of $_A$Hb, monitoring, $_T$Hb trending could have an interesting clinical impact, particularly when the anesthesiologist is confronted with an acute systemic variation of $_A$Hb. The authors conducted a prospective study to observe the variations of $_A$Hb inpatients before, during, and after cardiopulmonary bypass (CPB). $_T$Hb was monitored with the FORE-SIGHT™ cerebral oximeter[19] using the near-infrared spectroscopy (NIRS) technology. The first goal of this study was to evaluate the ability of the $_T$Hb to track variations of $_A$Hb during transitions from pulsatile to constant flow and conversely. The second objective was to evaluate the impact of $_A$Hb, hemodynamic and epidemiologic parameters on $_T$Hb.

METHODS

The protocol used was approved by the institutional review board for human subjects of Comite Consultatif de Protection des Personnes dans la Recherche Biomedicale Lyon Sud Est III (Ref: 2011-A00910-41). After receiving written informed consent, 30 patients scheduled for cardiac surgery using CPB were enrolled in a prospective observational study. The study was conducted by the Department of Anesthesiology and Intensive Care, at Louis Pradel Hospital, Hospices Civils de Lyon in Lyon, France over an 11-month period (from January 2012 to November 2012). Patients under 18 years of age were excluded.

After application of standard ASA monitors, all patients had a radial artery catheter placed for continuous measurement of systemic arterial pressure and blood draws for laboratory analysis. Patient characteristics [age, gender, body surface area, body mass index, ASA, Euroscore, and SCORE[20] (Systematic Coronary Risk Evaluation, to estimate the atherosclerotic disease)], surgical variables (type of surgery, operation time, CPB time, aortic cross-clamping time), and fluid balance (total volume intravenous fluids given, total volume of packed red blood cells transfused and renal output) were recorded. After the induction of general anesthesia, 2 dedicated probes were placed bilaterally on the forehead and then connected to the FORE-SIGHT™ cerebral oximeter (CAS Medical Systems, Branford, CT),[19] which utilizes the near-infrared spectroscopy (NIRS) technology. This device uses a laser light with four precise wavelengths to determine oxyhemoglobin and

*From the *Department of Anesthesiology and Intensive Care, and †Laboratory EA4169, Louis Pradel Hospital, Claude Bernard Lyon 1 University, Lyon, France; and ‡Department of Anesthesiology and Perioperative Care, University of California, Irvine, CA; §Department of Surgery, Louis Pradel Hospital, Claude Bernard Lyon 1 University, Lyon, France; ||Department of Anesthesiology and Intensive Care, Wertheimer Pierre Hospital, Claude Bernard Lyon 1 University, Lyon, France; ¶Hospices Civils de Lyon, Université Lyon I, Villeurbanne, and Service de Biostatistique, UMR 5558, Laboratoire Biostatistique Santé, Pierre-Bénite, France.*

Address reprint requests to Olivier Desebbe, MD, Louis Pradel Hospital, Department of Anesthesiology and Intensive Care, 28 Avenue du Doyen Jean Lepine, 69500 Bron. E-mail: oldesebbe@yahoo.com

1053-0770/2601-0001$36.00/0
http://dx.doi.org/10.1053/j.jvca.2013.06.026

deoxyhemoglobin changes in the frontal lobe using a modified Beer-Lambert law, which includes a constant but unknown light dispersion factor. This tissue oximeter provides online continuous cerebral tissue oxygen saturation ($SctO_2$, the ratio between oxyhemoglobin and deoxyhemoglobin) and offline total tissue hemoglobin concentration changes ($_T$Hb) per volume of brain tissue over time (concentration changes of oxyhemoglobin and deoxyhemoglobins were expressed in μmol/L). The precise algorithm used to determine $_T$Hb is the manufacturer's property. $SctO_2$ was displayed continuously starting after the induction of anesthesia until the end of the intervention. Postoperatively, data were downloaded from the cerebral oximeter using the "research-mode" setting. For this particular study, the software was provided by the manufacturer and recorded the value of $_T$Hb and $SctO_2$ from each frontal lobe every 2 seconds. Investigators downloaded and analyzed the data independently of the firm. For reference hemoglobin values, arterial blood samples were taken and analyzed with the CELL-DYN Sapphire® hematology analyzer (Abbott Diagnostics Division, Santa Clara, CA) to obtain hemoglobin concentration in blood (g/dL) and hematocrit (%). In addition, a conventional gas analysis was used to measure arterial partial pressure of oxygen (PaO_2) and arterial partial pressure of carbon dioxide ($PaCO_2$). Mean arterial pressure (MAP), heart rate (HR), central venous pressure (CVP), and temperature values also were collected as well as pump flow rate and venous oxygen saturation (SvO_2) during CPB. Measurements were studied at 3 defined time points during cardiac surgery: At the induction of anesthesia (T1), 10 minutes after administration of cardioplegia during CPB (T2), and at the end of the surgery (T3). Anesthetic and hemodynamics were managed at the discretion of the anesthesiologist. Patients were kept under mild hypothermic conditions (34-35°C) during CPB.

Routine demographic, procedure-specific data and hemodynamic variables were collected for each subject and stored into a database. All continuous variables were described with median (range or quartile) and categoric variables with numbers and percentages. The difference of hemodynamic parameters over time was tested separately using Friedman analysis of variance on ranks.. $_T$Hb and $SctO_2$ were calculated offline by averaging the right and left $_T$Hb and $SctO_2$ values, respectively, during each 2-minute interval. The time variability of $_T$Hb was evaluated by the coefficient of variation (CV_{THb}), expressed in percentage for each hemisphere during a 2-minute period at each step of the study. CV_{THb} was calculated as the standard deviation divided by the average of $_T$Hb. Since $_A$Hb and $_T$Hb are measured using different scales, the 2 variables were standardized for comparison. In order to study concordance between $_T$Hb and $_A$Hb, modified Bland and Altman plot graphs were drawn overall and in relation to time.[21] A linear regression and a 4-quadrant plot graph were performed to determine the concordance between variations of $_A$Hb (Δ_AHb) and variations of $_T$Hb (Δ_THb). This analysis determined trending ability and testing directionality of change. As the CELL-DYN Sapphire® hematology analyzer has a percentage of error in $_A$Hb measurement less than 1%, the exclusion zone was defined arbitrarily by changes in $_T$Hb lower than 5%. According to a previous result,[22] which showed a correlation of 0.53 between $_T$Hb and $_A$Hb, the authors calculated a sample size of 30 patients.

In order to study the relation between $_A$Hb and $_T$Hb while taking into account specific confounding factors, a linear hierarchical regression model was built. Apart from type of measure ($_T$Hb or $_A$Hb), other variables were considered for analyses and included: Time in 3 categories (T1, T2, T3), $SctO_2$, hemodynamic and respiratory parameters (MAP, $PaCO_2$, CVP), and epidemiologic data (age and SCORE). Hemoglobin concentration was modeled, and a random intercept was introduced to take into account the correlation of $_A$Hb and $_T$Hb results for the same patient. The parameter estimated for the type of hemoglobin was a quantification of the relation between $_A$Hb and $_T$Hb. In order to take into account the influence of time evolution of $_A$Hb and $_T$Hb, time was introduced as an interaction with type ($_T$Hb or $_A$Hb). Age and SCORE were adjustment variables. Assuming that hemodynamic parameters would only influence $_T$Hb, they were considered as an interaction term with $_T$Hb; no average specific effect was estimated. Although the values at 3 time points were considered for the hemodynamic parameters, no further interaction with time was introduced because of the complex communication about third-order interaction. All the other variables were first included individually to test their association with Hb adjusting on type, time, and the type-time interaction. Then, they were introduced in mutual adjustment. The level

Table 1. Demographic Data and Surgical Characteristics

Patient	
Age (y)	68 (29-89)
Body Surface Area (m²)	1.9 (1.5-2.3)
Body Mass Index (kg/m²)	26 (19-35)
ASA	3 (2-4)
EuroSCORE	4 (0-15)
SCORE risk	Low risk n = 4
	Medium risk n = 6
	High risk n = 20
Surgical Procedure	
Type of surgery	
Coronary artery bypass grafting	4
Valve surgery	18
Aortic ascending surgery	2
Combined surgery	5
Atrial septum defect closure	1
Length of surgery	
Operation time (min)	166 (69-302)
CPB time (min)	82 (32-209)
Aortic cross-clamping time (min)	55 (22-179)

NOTE. Data are expressed as median (range), for n = 30 patients.

Abbreviations: CPB, cardiopulmonary bypass; EuroSCORE, European system for cardiac operative risk evaluation; SCORE risk, systematic coronary risk evaluation (cardiovascular event at ten years < 1% if low risk, between 1 and 9% if medium risk, > 9% if high risk).

Table 2. Hemodynamic Variables, Arterial Blood Gas and Temperature During Surgery

	T1	T2	T3
HR (beats/min)	62 [56; 73]		76 [64; 90]
MAP (mmHg)	67 [63; 73]	61 [53; 67]*	69 [62; 74]*
Temperature (°C)	36.2 [35.9; 36,7]	34.8 [34.1; 35.5]*	36.5 [35.8; 36,8]*
PaO_2 (kPa)	22.4 [16.7; 26.7]	32.8 [29.4; 38.3]*	16.4 [11.3; 20,5]*
$PaCO_2$ (kPa)	5.2 [4.7; 5.6]	4.6 [4.3; 5.1]*	5.1 [4.6; 5.5]*
CVP (mmHg)	11 [8; 14]	6 [3; 12]*	12 [7; 17]*
CPB flow rate (L/min)		3.7 [3.5; 4.1]	
SvO_2 (%)		86 [83; 88]	

NOTE. Data are expressed as median [25%; 75%] for n = 30 patients.

Abbreviations : CPB, cardiopulmonary bypass ; CVP, central venous pressure; HR, heart rate; MAP, mean arterial pressure; $PaCO_2$, arterial partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; SvO_2, venous oxygen saturation.

*significant difference with $p < 0.05$, between T1 and T2, and T2 and T3.