Automatic Control of Gas Exchange During Cardiopulmonary Bypass

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ABSTRACT

An automatic control system was devised that regulates gas exchange during cardiopulmonary bypass (CPB). The Automated Extracorporeal Gas Exchange System (AEGES) controls the blood flow rate and/or the flow of gas to the oxygenator in order to meet user-defined setpoints for PO₂ and PCO₂ of blood drained from the patient while maintaining safe pressures in the CPB circuit and/or the patient’s circulation. Venous blood gases were used as the basis for control because they reflect the amount of oxygen/CO₂ consumed/produced by the patient given the present rate of delivery via CPB. In the event of an alarm or upon the perfusionist’s command, AEGES reverts to manual control of blood flow and/or sweep flow.

AEGES was tested in a hypothermia model of CPB in sheep, where it successfully regulated PO₂ and PCO₂ within 5% of setpoint during cooling from 38 to 25°C. In order to control the blood gases to setpoints of PO₂=45 mmHg and PCO₂=40 mmHg in the venous drainage, AEGES reduced blood flow from 2.4 to 1.6 L/min and sweep flow from 2.2 to 0.7 L/min.

AEGES is intended to act as a tool for the perfusionist to assist in maintaining consistent blood gas conditions. AEGES can be integrated with other control systems (e.g., reservoir level control and blood temperature control), further automating the CPB procedure; however, in no way could this system replace the perfusionist.

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INTRODUCTION

A strategy was developed for regulating gas exchange during cardiopulmonary bypass (CPB) while maintaining safe operation by ensuring safe pressures within the CPB circuit, providing sufficient perfusion to maintain the patient's arterial blood pressure, and preventing the emptying of the venous reservoir. The control strategy involved continuous feedback control of the arterial blood pump speed and the rate of gas flow through the oxygenator (Q\textsubscript{pre}). Control was used to maintain desired blood gas chemistry in mixed venous blood, which is an indicator of the gas exchange needs of the patient. Post-oxygenator blood gases were also measured to audit oxygenator function and to ensure safe blood gas chemistry of infused blood. The automated extracorporeal gas exchange system (AEGES) was designed as a tool for perfusionists to facilitate automated adjustment of system parameters in response to a patient's varying gas exchange demands during CPB or prolonged extracorporeal life support (e.g., ECMO).

Several aspects of CPB are enhanced by the use of automatic control: the level of blood in the reservoir is controlled using level sensors, blood temperature is regulated by a blood warmer/cooler, and feedback control ensures that the pressure within the extracorporeal circuit does not exceed dangerous levels. Despite the prevalence of automatic control technology, gas exchange, a primary function of the CPB system, has not been automated. The gas exchange requirements of the patient vary widely during a procedure. The perfusionist can make adjustments to the CPB system to regulate the rate of oxygen delivery and carbon dioxide removal, but the perfusionist generally has many other responsibilities that preclude his/her focusing continuously on making such adjustments. Optimizing gas exchange while tracking indicators of safe system operation is best accomplished by continuous monitoring, which is efficiently performed by a computer.

The reason for the development of automatic control of gas exchange was a desire to address fluctuations in gas exchange requirements of a patient during CPB. Changes in metabolic rate due, for example, to anesthesia and hypothermia, can greatly alter a patient's need for oxygen delivery and CO\textsubscript{2} removal. Investigators have reported detrimental effects of even brief periods of hypoxia or hypercapnia during CPB (1, 2).

Automated control of gas exchange has been described previously, but none of the presented strategies has been incorporated into the popular standard for CPB. Control of post-oxygenator blood gas chemistry (PaO\textsubscript{2} and PaCO\textsubscript{2}) is beneficial for maintaining cerebral blood flow (1, 3). Systems have been described that control post-oxygenator blood gases by adjusting the flow and composition of gas supplied to the oxygenator (4, 5, 6), which can be advantageous in preventing high PO\textsubscript{2} and low PCO\textsubscript{2} values of infused blood. However, these systems do not respond to variations in patient gas exchange requirements, which are reflected by venous blood gases (PvO\textsubscript{2} and PvCO\textsubscript{2}). Control of venous blood gases has not been discussed despite evidence that low venous oxygen tension during CPB is an indication of hypoxic acidosis (2).

The control strategy presented here involves the regulation of pump speed (i.e., extracorporeal blood flow) and Q\textsubscript{pre}, in order to adjust O\textsubscript{2} delivery and CO\textsubscript{2} removal to meet the gas exchange requirements of the patient, as quantified by the PO\textsubscript{2} and PCO\textsubscript{2} of mixed venous blood. Oxygen delivery is the product of blood flow and blood oxygen content. Adjusting blood flow provides the greatest control of oxygen delivery in CPB because post-oxygenator O\textsubscript{2} content is effectively constant (i.e., 100% oxygen saturation), as oxygenators are sufficiently efficient to fully oxygenate blood over the entire range of CPB blood flows. Blood flow can be adjusted to regulate oxygen delivery, as long as blood flow is sufficient to maintain the desired arterial blood pressure and is below the level that would cause the reservoir to empty or would create excessive pressures in the CPB circuit.

Q\textsubscript{pre} is used to control CO\textsubscript{2} removal, because the sweep flow rate determines the rate of CO\textsubscript{2} removal in the oxygenator due to the rapid diffusion of CO\textsubscript{2}. In control of Q\textsubscript{pre}, the range of possible values is limited by post-oxygenator blood gases: PaO\textsubscript{2} and PaCO\textsubscript{2} must be kept within a determined range of safe values. Both extracorporeal blood flow and sweep flow indeed affect both O\textsubscript{2} delivery and CO\textsubscript{2} removal, so it is not purely a matter of one control output regulating one control variable. However, it was supposed that blood flow could be used to regulate oxygen delivery and sweep flow could be used to regulate CO\textsubscript{2} removal to a reasonable approximation, if limits were observed. A diagram of the control system is presented in Figure 1, showing the sensors used to measure and transfer data to the controller and the signals output from the computer to the blood pump and gas flow controller.

MATERIALS AND METHODS

The controller was rendered in a microcomputer-based system. Figure 1 shows the configuration of sensors used as inputs to AEGES and the control signals output to the gas flow and pump speed controllers. A laptop computer was equipped with an I/O board. One A/D channel read extracorporeal blood flow as measured by an ultrasonic blood flowmeter, and another A/D channel read pre-oxygenator circuit pressure. A gas flow controller calibrated for oxygen flows from 0 to 10 L/min was controlled by one D/A output, and included a thermal diffusion flowmeter to verify sweep gas flow rate. Another D/A output was connected to the speed controller of a roller pump. Blood gas concentrations were measured continuously using the CDI 300 which communicated with the computer through a serial port.

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The control system software was developed using the Visual Basic 4.0 programming environment. The computer read the blood gas values and calculated a new pump speed and gas flow according to a control algorithm. Limits on control variables (e.g., pump speed) were user-definable to maintain control variables within a safe range. It was also possible for the user to override one or both controllers for manual operation. The computer monitored blood flow, reservoir level, pressures within the CPB circuit, the patient’s arterial blood pressure, and gas flow supplied to the oxygenator, and the controller overrode the calculated blood and gas flows if any parameters were out of range. For example, if the \( P_{vO_2} \) rose above the setpoint, the pump would slow down, thereby decreasing oxygen delivery, unless the arterial blood pressure fell below its setpoint, in which case the pump speed would be adjusted to meet the desired pressure. Similarly, if the reservoir level approached the safety level, the controller would decrease blood flow even though the \( P_{vO_2} \) value was below setpoint. This protocol resulted in control of gas exchange only when the system was operating within defined pressure, level and flow limits; perfusionist intervention was required when these limits were reached.

Additional safety features included a user override so the perfusionist could readily revert to manual control. Alarms warned the perfusionist if any measured parameter was outside of user-defined limits or if the controller reached the limits of its control signal outputs. Under alarm conditions, the controller automatically switched to manual control and awaited the attention of the perfusionist.

The main control panel of the user interface is shown in Figure 2. The control panel is divided into three main sections: oxygen delivery, \( CO_2 \) removal, and alarms. In the oxygen delivery section, the user can read the current \( P_{vO_2} \), blood flow, and pump speed. The user then selects manual or automatic control of pump speed, and enters a setpoint for pump speed (manual mode) or \( P_{vO_2} \) (automatic mode). In the \( CO_2 \) removal section, the user can read the current \( P_{vCO_2} \), gas flow, and percent opening of the \( Q_{gas} \) control valve. The user then enters a setpoint for gas flow (manual mode) or \( P_{vCO_2} \) (automatic mode). An additional option for automatic gas flow control is possible, where the controller sets \( Q_{gas} \) equal to a user-entered constant times the measured blood flow. The alarm section warns the perfusionist if input data are out of range or if control limits have been reached. Additional control windows display control data graphically and allow the user to enter alarm and control limits and to log or print data.

In order for the controller to compensate for changes in gas exchange requirements of the patient in the least amount of time and without causing excessive fluctuations in blood and sweep flow rates, the response time of the sensor plus patient system needed to be measured. The response times of blood gas sensors used with the controllers were measured in vitro, and agreed roughly with reported values (7). The time constant (time to reach 63.2% of the total response following a step input) for the CDI sensors was approximately 2.5 minutes for \( P_{vCO_2} \), and 1.5 minutes for \( P_{vO_2} \). The sensor response times were assumed to be much larger than the dynamics introduced because of circulation times and mixing of infused blood. A time delay is present in the system due to the finite transit time of blood between the patient and the CDI sensors. The system dynamic characteristics were used to develop a simple system model that was used to design a control algorithm with the desired time response. The goal was to design the controller such that disturbances to the system (i.e., changes in gas exchange) would be compensated for in a reasonable time, such as a return to within 5% of the setpoint value within 5 minutes. The controller also should not overshoot the setpoint when making a correction. Most importantly, the controller was required to be stable under all conditions. The definition of stability in this context is that the controller should never cause excessive variation in the control signals that would result in oscillation between the minimum and maximum allowable values. Instability can occur if the control algorithm is based on an inaccurate system model.

**In vivo evaluation in sheep:** The AEGES was evaluated in two sheep (approximately 25 kg) placed on CPB. All animals used in this study received humane care according to NIH guidelines. The animals were anesthetized, mechanically ventilated,
instrumented, and prepared for CPB. After anticoagulation with bolus injection of heparin (300 IU/kg), the internal jugular vein was cannulated with a 25F catheter for drainage and the common carotid artery was cannulated with a 17F catheter for infusion. ACT was checked approximately once an hour and intravenous heparin administered to maintain the ACT > 400 secs. A CPB circuit was constructed of PVC tubing, an oxygenator with integral heat exchanger and a non-occlusive roller pump. CDI 300® arterial and venous sensor cells were placed in-line post- and pre-oxygenator, respectively, following two-point calibration with standard gas blends. The circuit was primed with crystalloid and sheep blood to yield a final hemoglobin concentration of approximately 5 g/dl. Heparin (1000 IU) and calcium chloride (750 mg) were administered to the circuit and additional doses administered to achieve an activated clotting time (ACT) > 400 seconds and ionized calcium > 1.1 mmol/L. The water heater was adjusted to achieve a perfusate temperature of approximately 37°C.

CPB was initiated, and limits were defined for system settings and for alarms to ensure safety. Qₑ was limited to between 0.1 and 7.0 L/min in order to meet specifications defined by the oxygenator manufacturer. Limits of 10% to 60% were entered in the AEGES as the range of possible pump speeds; these speeds corresponded to CPB blood flow values of 0.1 to 3.5 L/min. The blood pump used in this application was passively filling; hence, reservoir level control was effected by placing the inlet of the pump at the safety point of the reservoir, ensuring that the reservoir level would never fall below the safety level, as described previously in this journal (8).

Adjustments were necessarily made to parameters in the control algorithms in order for the closed loop system to have the desired response (i.e., sufficiently rapid response and no overshoot of setpoint). Tuning of a control system is commonly performed by observing the response of the open loop system to changes in the control variables. Knowing the open loop response, established techniques for controller tuning can be employed (9). The open loop responses in this application involved observing changes in system variables following sudden (step) changes in blood flow and gas flow. Closed loop step responses were verified both with increasing and decreasing changes in setpoint to ensure stability. The tuning of the controllers was dependent on the response of the blood gas sensors. Using this system with other blood gas sensors would require additional tuning or the use of techniques to adjust the controller dynamics automatically.

Tuning of the controllers was performed to customize the controllers based on the dynamics of the system to be controlled. However, the system dynamics vary considerably depending on several conditions. As blood flow is decreased, circulation time, and hence the time required for blood to reach the blood gas sensors, varies, resulting in changes in time delay. The gain of the system also changed with temperature, because of changes in the relationship between oxygen delivery and consumption. Accordingly, controller parameters were defined as a function of blood flow to compensate for variations in time delay because of changing time delays for low blood flows. The system gain also fluctuated with temperature because of changes in the CDI sensor response time and the change in the gain of the oxygen delivery/oxygen consumption relationship.

The performance of AEGES was observed and recorded during initiation of CPB in order to examine the ability of the controller to properly adjust blood flow and Qₑ when the ventilation ceased and total bypass commenced. AEGES was also evaluated following interventions designed to vary the metabolism of the sheep. For example, the core temperature of the animal was rapidly decreased from 38°C to 25°C and then returned to 38°C using a blood warmer/cooler.
RESULTS

The AEGES was found to be capable of controlling gas exchange in CPB effectively, both in the initiation of CPB and during variations in the core temperature of the sheep. Figure 3 shows the results of an experiment in which a 33 kg sheep was placed on CPB, using AEGES. The plots show the 8.5 minutes following the initiation of total bypass. The PVo₂ setpoint was set to 39 mmHg, and the PvCO₂ setpoint was 51 mmHg. Baseline CPB blood flow was established as 1.7 L/min, and the controller was switched to automatic mode. The controller increased the pump speed and brought the PVo₂ to the setpoint in less than 4 minutes with no overshoot (upper plot in Figure 3). Similarly, AEGES increased Qgas from 2 to 5.5 L/min, and was able to return PvCO₂ to the setpoint of 51 mmHg in 5.5 minutes following a rise in PvCO₂ (lower plot in Figure 3). Post oxygenator PO₂ was maintained between 400 and 450 mmHg during this period.

In the hypothermia experiment, AEGES was able to regulate PVo₂ and PvCO₂ to within 5% of setpoint during cooling to 25°C and during rewarming to 38°C. The setpoint for PVo₂ was 45 mmHg, and the setpoint for PvCO₂ was 40 mmHg. To achieve these blood gas values, AEGES reduced blood flow from 2.4 to 1.6 L/min and Qgas from 2.2 to 0.7 L/min. Control during cooling was complicated by variations in the system response time with lower temperatures, and more deviation of the control variables from their setpoints was observed.

DISCUSSION

AEGES was originally designed for prolonged extracorporeal membrane oxygenation (ECMO), but its application to CPB is discussed here. It was demonstrated that the rates of oxygen delivery and CO₂ removal can be regulated by adjusting CPB blood flow and Qgas, respectively. Variations in venous blood gases were observed following interventions that changed metabolic requirements of a sheep, and AEGES was able to adjust gas exchange rapidly and accurately to return the venous blood gases to their desired levels.

It is important to recognize the challenge in manually controlling a feedback system using sensors with slow response times when the system never reaches true steady state. This case presents a further challenge in that the various sensors have different response times and because a time delay exists between adjustments made to the system (e.g., pump speed) and the response of control variables (e.g., PVo₂). An experienced user can develop an intuitive feel for the magnitude of a change based on the rate of change of a value on the blood gas monitor and anticipate the necessary correction, but only through continuous observation. If a perfusionist looks at the continuous blood gas sensor, he or she may be seeing the blood gas conditions of two minutes ago, and will not see the complete effects of a change in gas exchange for as long as five minutes. Furthermore, the perfusionist cannot immediately see the effects of a change to blood flow or sweep flow, hence he/she can not be sure of the magnitude of the necessary adjustment, thereby requiring further adjustment a couple of minutes later.
AEGES is one of several tools at the disposal of the perfusionist. It can be thought of as an auto-pilot or cruise control system for gas exchange in CPB: the system can run efficiently while the perfusionist attends to other responsibilities, but requires a perfusionist who can assume manual control when the control system reaches its limits or senses a problem. For example, if it is impossible for the AEGES to increase CO₂ removal, the perfusionist must determine whether the oxygenator has failed or if the gas and blood flow specifications of the oxygenator have been exceeded.

AEGES was shown here to be capable of controlling gas exchange during CPB. It is anticipated that such control will be of particular importance during the initiation of bypass and during the weaning process. While AEGES in no way replaces the perfusionist, it may represent an effective tool for reacting to the patient’s varying gas exchange requirements during CPB.

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REFERENCES