Utility of an Implantable Right Ventricular Oxygen Saturation-Sensing Pacemaker for Ambulatory Cardiopulmonary Monitoring*

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Mixed venous oxygen saturation (SvO₂) is a physiologic parameter reflecting cardiac output (CO) and tissue oxygen utilization. An implantable oxygen sensor incorporated in a right ventricular pacing lead has been developed to assess the feasibility of ambulatory monitoring of SvO₂ to predict cardiorespiratory parameters. Eight patients with a mean age of 62 ± 2 years and sinoatrial disease received an SvO₂-driven dual-chamber rate-adaptive pacemaker capable of continuous SvO₂ measurement. During graded maximal exercise with measurement of oxygen consumption (VO₂), arterial oxygen saturation (SaO₂), and telemetered derived SvO₂ data, CO was assessed using the Fick principle. The accuracy of the derived CO was compared with CO measured directly by continuous-wave Doppler assessment of the ascending aortic flow. The maximum changes in SvO₂ and SaO₂ during exercise were 25 ± 5 and 3 ± 1%, respectively. SvO₂ was significantly correlated with VO₂ (r=0.9 ± 0.1, p<0.001), work done (r=0.8 ± 0.1, p<0.05), and minute ventilation (r=0.9 ± 0.1, p<0.05). Doppler-derived CO was significantly correlated with CO estimated from SvO₂ measured (r=0.8 ± 0.1, p<0.05) and is expressed as 46X derived CO +300. Although continuous SvO₂ sensing was originally developed to increase pacing rate during exercise, its use can be extended for monitoring cardiopulmonary performance on an ambulatory basis. This may be useful as a direct assessment of cardiopulmonary status in diseased states and also as an objective means to evaluate cardiac response to medical therapy in patients with heart failure.

Key words: mixed venous oxygen saturation; pacing; intensive monitoring

A variety of implantable sensors have been used to provide a rate response during exercise in chronotropically incompetent patients.¹ These sensors either employ the physical principle of sensing intrathoracic impedance (minute ventilation and stroke volume), paced intracardiac electrogram (paced QT interval and depolarization gradient), or acceleration changes in the pacemaker (body movement sensing) during exercise. In addition, a few sensors have been incorporated into specialized pacing leads, allowing intracardiac physical (eg, temperature, pressure) and chemical events (eg, mixed venous oxygen saturation [SvO₂], pH) to be detected. The physiologic parameters derived from these sensors may not only provide data to increase pacing rate, but also for purposes other than rate augmentation. Uses such as the management of supraventricular tachyarrhythmias,² automatic sensing and pacing assessments,³,⁴ optimal atioventricular interval, and postventricular atrial refractory period have been proposed or implemented. In addition, there is also the possibility of utilizing sensors for monitoring purposes such as to detect cardiac allograft rejection⁵,⁶ and to diagnose hemodynamically unstable ventricular tachycardia in tiered implantable defibrillator therapy.⁷,⁸

Arteriovenous oxygen saturation difference is dependent on the oxygen consumption (VO₂), cardiac output (CO), and oxygen-carrying capacity of blood. Provided that arterial oxygen saturation (SaO₂) is known, SvO₂ is a useful reflection of cardiovascular performance in critically ill patients⁹,¹⁰ However, the current monitoring technique requires the insertion of a pulmonary arterial line and precludes the possibility of long-term monitoring of SvO₂. With the development of a long-term implanted SvO₂ sensor for rate-adaptive pacing,¹¹-¹⁴ the possibility of using an implantable SvO₂ sensor for ambulatory SvO₂ monitoring of cardiovascular performance was assessed.

OXYGEN SENSING LEAD AND PACEMAKER

Oxygen Sensing Lead

A unipolar polyurethane steroid-eluting ventricular pacing lead was custom modified for SvO₂ sensing (model 4327, Medtronic Inc, Minneapolis). At 25
mm from the ventricular pacing electrode, an oxygen sensor is incorporated that detects $SvO_2$ by the principle of reflectometry. The technical details of the $SvO_2$ sensor have been reported. In brief, it consists of red (660 nm) and infrared (880 nm) light-emitting diodes, hermetically sealed in a sapphire capsule. The reflectance of the light from each is received and measured by a photodetector to generate a relative reflectance ratio. This ratio varies in proportion to changes in right ventricular $SvO_2$. The use of a reflectance ratio instead of reflectance from a single wavelength has been shown to reduce the variation in $SvO_2$ determination resulting from fibrin coating, intrasystolic variation, velocity of blood flow, ventricular wall proximity, and changes in hematocrit. The $SvO_2$ was sampled, once every 4 s, synchronized to an R wave. The lead is connected to the pacemaker via an IS-1 in-line “bipolar-like” (unipolar ventricular pacing and sensing, $SvO_2$ parameters) connection.

**Dual-Sensor Dual-Chamber Rate-Adaptive Pacemaker**

The pacemaker (OxyElite, model 8007, Medtronic Inc) is based on an activity-sensing DDDR pacemaker from the same manufacturer (Elite II, model 7086). It can be programmed to provide rate response either using a right ventricular $SvO_2$ sensor or a piezoelectric activity sensor. The pacemaker features both activity and $SvO_2$ telemetry (in real time), and it will also collect data for programmer display and storage of $SvO_2$ values. On-line sensor data can be obtained by telemetry even in the DDD mode with the sensor programmed passive.

Because patients have different levels of $SvO_2$ at rest, the “resting rate offset” (1-31, in steps of 1) is used to establish the point from which oxygen rate response can begin as well as the desired pacing rate at rest. Once the resting rate offset is exceeded, the desired rate response can be programmed using a rate response curve, the so-called “oxygen rate response” (1-16, in steps of 1). A linear relation is used to relate a change in $SvO_2$ to a change in rate (bpm/O2%). For the purpose of this study, the DDD mode was used, and only telemetry-derived $SvO_2$ level was used for analysis.

**Pacemaker Implantation and Sensor Validation**

The implantation was similar to a conventional DDD pacemaker. As the position of the sensor precludes the passage of a stylet guidewire to the tip of the ventricular lead, more manipulation of the lead into the right ventricle was required. A satisfactory pacing and sensing position for both leads was achieved in all patients, with the sensor well within the right ventricular body. In five patients, a simultaneous right ventricular blood sample was taken to correlate with the telemetered derived $SvO_2$ level (Fig 1).

**Methods**

**Patients**

Eight female patients with symptomatic sinoatrial disease received the dual-sensor DDDR pacemakers. All gave informed written consent to participate in this study which was approved by the local ethics committee. Their mean age was 62 ± 2 years and all had normal left ventricular systolic function and normal aortic valve on echocardiography. Results of lung function tests were within normal limits in all patients. Associated cardiac diseases are hypertension with left ventricular hypertrophy, and atrial arrhythmias (one exercise-induced atrial fibrillation, one persistent atrial tachycardia after atrioventricular nodal ablation).

At 1 month after implantation, patients underwent an initial familiarization exercise test on the treadmill. One week after this test, cardiopulmonary exercise testing was carried out. Exercise testing was continued until patient exhaustion. The experimental set-up is illustrated in Figure 2.

**Figure 1.** Anteroposterior (AP) and left anterior oblique (LAO) radiographs of a patient during implantation of an oxygen-driven dual-chamber rate-adaptive pacemaker. The oxygen sensor was shown up radiographically as three radiopaque dots (lower arrows) proximal to the ventricular pacing electrode. A 6F multipurpose catheter (upper arrow) was advanced from the femoral vein into the right ventricle for simultaneous blood sampling.
Cardiopulmonary Exercise Testing

Graded treadmill exercise testing was performed using the "chronotropic assessment exercise protocol." This protocol involves a gradually increasing work load in 2-min stages in a linear fashion, especially covering the low exercise level to cater for the less athletic pacemaker recipients.

During treadmill exercise test, VO2 was continuously measured with a breath-by-breath analysis, using a metabolic cart (model 2900 MMC, SensorMedics, Anaheim, Calif.). Gaseous flow and volume are measured using a mass flow sensor that has monotonic curvilinear output characteristics as a function of flow, with the highest sensitivity at low-flow values. The resolution in detecting tidal volume changes is about 15 mL. Oxygen is analyzed using a zirconium oxide sensor with a fast response to changes in oxygen saturation (typically within 120 ms). The oxygen level is calibrated with 16% and 26% oxygen using a two-point calibration scheme. Carbon dioxide is measured using the principle of non-dispersive infrared absorption technique. Carbon dioxide is passed through a sample cell in the path of infrared energy, and changes in the electrical signal are proportional to the carbon dioxide partial pressure. During a breath-by-breath assessment, the gas flow and partial pressures of oxygen and carbon dioxide are sampled at a frequency of 125 Hz, and the values are summed and averaged for each breath. A moving average of 20 s was used in the assessment of respiratory variables of VO2 tidal volume, minute ventilation, carbon dioxide production, and respiratory rate. The system is integrated with an exercise treadmill (Quinton 5000, Seattle) and a pulse oximeter (Sat-Trak, SensorMedics) to derive SaO2.

Cardiac Output Measurement

During exercise, ascending aortic blood flow was measured by continuous-wave Doppler at rest and at the end of each stage of exercise testing. The Doppler ultrasound unit (Exerdop, Quinton) samples the ascending aortic blood flow using a continuous-wave transducer and receiver at 3 MHz placed at the suprasternal notch. The systolic velocity integral (also known as the stroke distance in centimeters) reflects the distance traveled by a column of blood in the aorta during systole. The minute distance (also in centimeters) is the product of heart rate and stroke distance. As the cross-sectional area of the ascending aorta remained relatively unchanged during exercise, the minute distance thus represents the CO. The proprietary circuit rejects noise and excludes ectopic beats, and an average of 10 beats was used to represent the instantaneous CO during exercise. The reproducibility of sampling ascending Doppler flow using this technique has been published.

Data Analysis

Estimation of CO: Using the Fick principle for oxygen uptake,

\[
CO = \frac{V_{O2}}{[Sao2 - SvO2] \times 1.34 \times \text{hemoglobin}}
\]

where CO = cardiac output, \(V_{O2}\) = oxygen consumption (in mL/kg), and SaO2 and SvO2 are the percentages of arterial (from pulse oximeter) and mixed venous (from pacemaker telemetry) oxygen saturation. Assuming hemoglobin level remained unchanged during exercise, CO can be derived (in units) using the above equation with \(V_{O2}\) and oxygen saturation values alone.

Linear Regression: Linear regression was performed between SvO2 and VO2, SVo2 and work load, and SVo2 and minute ventilation at each stage of exercise. This test was also used to relate directly measured (from Doppler) and CO estimated from oxygen saturation. Pearson product moment correlation coefficients (r) were derived between the derived and estimated CO. All results are expressed as mean ± SEM. A p value of <0.05 was considered statistically significant.

RESULTS

The SvO2 level from the sensor at rest was within 2% of the simultaneous blood gas value. One patient had suboptimal sensor function immediately after implantation, and she was excluded from the exercise test. Respiratory gaseous exchange could not be performed in another patient for technical reasons. The remaining patients completed the study. Exercise was limited either by dyspnea or fatigue in all patients.

The changes in cardiac, respiratory, and oxygen saturation parameters are summarized in Table 1. The duration of exercise testing and work performed are 10.2 ± 0.8 min and 55 ± 7 W, respectively.

Figure 3 shows the changes of SvO2 during exercise in each patient. As the arterial oxygen saturation changed only minimally during exercise, arteriovenous oxygen saturation difference was mainly reflected by the changes on SvO2. Mixed venous oxy-
gen saturation was linearly correlated with the minute distance (r=0.83 ± 0.03, p<0.05), V̇O₂ (r=0.93 ± 0.04, p<0.01), minute ventilation (0.87 ± 0.10, p<0.05), and work done (0.87 ± 0.10, p<0.05) at each stage of exercise.

The directly measured Doppler derived CO is a linear function of CO derived from arteriovenous oxygen saturation difference and V̇O₂ (Fig 4). At any point in exercise, minute distance in meters could be derived from the estimated CO (46.3 ± 10.7X estimated−CO+299.5 ± 138.4, r=0.77 ± 0.10, p<0.05) or from SvO₂ value (−25.2 ± 0.67X SvO₂+2,435 ± 471, r=0.83 ± 0.03, p<0.05).

**DISCUSSION**

**Main Findings**

This study examined the feasibility of using an implanted oxygen sensor to predict cardiopulmonary performance during exercise. A highly significant correlation between changes in SvO₂ and CO, V̇O₂, minute ventilation, and work performance was found. Using exercise as a physiologic stress to increase CO, it was shown that changes in CO could be predicted from SvO₂ value on an ambulatory basis.

**SvO₂ as a Monitor for Cardiovascular Function**

In patients with impaired cardiac function, oxygen delivery to the tissues will be reduced, resulting in a widening of arteriovenous oxygen saturation difference. A major goal in the treatment of these patients is to improve oxygen delivery in accordance with V̇O₂. Oxygen delivery to the tissue is commonly measured by a floatation pulmonary artery catheter using the thermodilution principle. However, this technique may be limited in low-flow states or in the presence of tricuspid regurgitation and may cause undesirable volume expansion during repeated cardiac output sampling. In addition, cardiac output measurement alone may not reflect the interaction between tissue oxygen uptake and extraction. Thus, SvO₂ has been suggested to be an alternative parameter to gauge oxygen delivery and uptake. In the intensive care setting, SvO₂ has been shown to be a useful indicator of CO, particularly if normalized for oxygen uptake and hemoglobin level.9,10,21-30 These studies used either intermittent blood sampling for the pulmonary artery or fiberoptic method for SvO₂ measurement, and could not be used in the ambulatory patients.

The development of implantable sensors for rate augmentation has now made an implantable SvO₂ sensor a possibility. This study shows the usefulness of SvO₂ to predict CO during exercise. The SvO₂ data can be derived noninvasively and stored in the pacemaker memory over an extended period of time. Thus, it may be possible to use such data for monitoring progress and response of patients with impaired heart function to therapeutic measures. Only exercise was used as a stress to the cardiopulmonary function, and the range of SvO₂ changes was relatively moderate in this group of patients with normal left ventricular performance. However, it has been reported that the accuracy of SvO₂ to predict cardiac

**Figure 3.** Changes in telemeter-derived SvO₂ during exercise in seven patients (901 to 908). Patient 906 had suboptimal sensor function and was excluded from exercise.

**Figure 4.** Correlation between CO estimated from V̇O₂, SvO₂, and SaO₂ arterial oxygen saturation (Est-CO in arbitrary units) and directly measured CO from Doppler (Dop-CO). Each dotted line shows 1 SEM from the mean.
index is even higher at low-resting SvO₂, for example, in patients with severely impaired left ventricular performance.29,30 More recently, an implantable sensor to detect pressure in the pulmonary artery has been used in patients with advanced heart failure prior to cardiac transplantation.31 On a different frontier but pathophysiologically similar, SvO₂ monitoring has been shown to be useful to predict circulatory collapse during malignant ventricular tachyarrhythmias.7,8

**SvO₂ as a Sensor for Rate Augmentation**

SvO₂ showed significant linear relationship to VO₂, minute ventilation, and workload. All these variables have a high correlation to heart rate. Although not a primary end point of this study, these results suggest the usefulness of SvO₂ for use in rate optimization as shown in previous studies.11-14,32

**Limitations of Study**

This study has evaluated only the short-term performance of the sensor to monitor SvO₂. For such a sensor to be useful to monitor ambulatory cardiopulmonary performance, its long-term stability requires more extensive evaluation. In a follow-up of a similar SvO₂ sensor, Faerestrand and Ohm12 reported 1 of 14 sensor failures in a 15-month follow-up. One of our eight patients had a suboptimal sensor function, which might be related to the burying of the sensor into the ventricular myocardium, as reported separately.14 The change in SvO₂ value derived from the sensor was only relative, and an invasive calibration will be required to reflect the actual SvO₂ value during exercise, although the changes in relative SvO₂ did correlate with CO changes. Inadequate mixing of venous blood cannot be excluded from the present study, although other investigators11,13 have reported adequate mixing of venous blood as sampled in the right atrium. We have ensured the sensor was within the right ventricle during implantation and during subsequent echocardiogram.

**Conclusion**

Implantable sensors for rate-adaptive cardiac pacing may be used for purposes other than rate augmentation. SvO₂ sensing, with its close association to cardiopulmonary performance and tissue oxygen extraction, showed promise to be a useful parameter for monitoring cardiopulmonary performance in ambulatory patients.

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