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Evaluation Of Mixed Venous Oxygen Tension As An Estimate Of Cardiac Output In Anesthetized Horses

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EVALUATION OF MIXED VENOUS OXYGEN TENSION AS AN ESTIMATE OF CARDIAC OUTPUT IN ANESTHETIZED HORSES

By

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ABSTRACT

EVALUATION OF MIXED VENOUS OXYGEN TENSION
AS AN ESTIMATE OF CARDIAC OUTPUT
IN ANESTHETIZED HORSES

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The relationship between mixed venous O_2 tension and cardiac output was studied in six anesthetized horses breathing 100 percent O_2. Cardiac output, O_2 consumption, mean arterial pressure, heart rate, and arterial and venous blood gases were measured after administration of xylazine or dobutamine to horses in lateral, sternal and dorsal recumbencies. At the end of the approximately three-hour experimental period, Escherichia coli endotoxin was administered while horses were in dorsal recumbency, and all measurements were repeated. Relationships between cardiac index (CI) and $P\bar{v}_{O_2}$, heart rate, mean arterial pressure, jugular Pv_{O_2}, and Pv_{O_2} of blood from a superficial limb vein were evaluated by linear regression analysis. Mean arterial pressure was significantly ($P< 0.05$) correlated with CI in horses in all positions and after endotoxin administration. However, data points were poorly grouped. Heart rate and CI were significantly

correlated in all horses in all positions but not after endotoxin administration. The correlations between jugular P_{VO_2} and P_{VO_2} of blood from a superficial limb vein were not significant in horses in sternal recumbency, and P_{VO_2} of blood from a superficial limb vein was not significantly correlated with CI in horses in lateral recumbency. There was a significant and tight correlation between $P\bar{v}_{O_2}$ and CI in horses in all positions and after endotoxin administration.

DEDICATION

To my mother,

Hanna Ivory Wetmore

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

A decrease in cardiac output is in part responsible for complications related to equine anesthesia including post-anesthetic recumbency myopathy and increased alveolar-arterial oxygen tension differences. Horses that require emergency anesthesia for repair of acute gastrointestinal or reproductive disorders frequently have concurrent hemodynamic instability. In all these cases, intraoperative monitoring of cardiac output is desirable.

Cardiac output in the horse has been measured directly and indirectly. Direct measurement of cardiac output is not clinically applicable. Indirect measurements of cardiac output have been made using indicator dilution methods and the Fick principle. Indicator dilution measurements of cardiac output are not routinely performed on anesthetized horses because these measurements require specialized equipment and technical familiarity with catheter placement and use of the equipment. Measurement of cardiac output (CO) using the Fick principle requires measurement of oxygen consumption ($\dot{V}O_2$) and the oxygen content of arterial and mixed venous blood.

$$CO = \frac{\dot{V}O_2}{\text{arterial } O_2 \text{ content} - \text{mixed venous } O_2 \text{ content}}$$

Where the content of oxygen (C_{O_2}) in mixed venous or arterial blood is calculated from the following formula requiring hemoglobin content in gm/100 ml blood (Hb), the O_2 saturation of the hemoglobin (S_{O_2}) and the oxygen tension in the blood (P_{O_2}).

$$C_{O_2} = (S_{O_2} \times Hb \times 1.34) + (P_{O_2} \times 0.003)$$

Measurement and calculation of these variables is too cumbersome for routine clinical use.

In a steady state a decrease in CO is accompanied by a decrease in $S\bar{v}_{O_2}$ and $P\bar{v}_{O_2}$ if oxygen consumption and arterial oxygen content remain constant.

The purpose of the present study was to investigate the use of $P\bar{v}_{O_2}$ in the estimation of CO in anesthetized normal horses and in horses given a bolus of Escherichia coli endotoxin. In addition, I examined the variability of oxygen consumption in anesthetized horses because this variability might interfere with the use of $P\bar{v}_{O_2}$ in the estimation of CO.

LITERATURE REVIEW

1. Cardiac Output Measurements in Horses

Cardiac output in the horse was first measured using the Fick principle (Zuntz and Hagemann, 1892). Blood was taken from an artery and from the right ventricle and blood gas analyses were performed. Oxygen consumption was determined by examination of expired air. From these measurements a value of approximately 75 ml/kg/min was calculated. Cardiac output measurements in horses were not reported again until 1961 when Fisher and Dalton described results of a study using an indicator dilution method previously employed in other species. Dye (Evans blue 20 mg/ml) was injected into the jugular vein over four seconds at a dose of 1 ml/50 kg body weight. A series of arterial blood samples were then collected from the brachial artery. Analysis of the dye content in these samples was done and cardiac output was calculated. Using fourteen horses the mean cardiac output value was again 75 ml/kg/min. Over the following fifteen years dye dilution studies for determination of cardiac output in horses were repeated with variable results (Table 1). It wasn't until 1976 that a thermodilution method for cardiac output determination was described in horses (Muir, Skarda, and Milne, 1976). Cardiac output was measured in each horse by both dye dilution and thermodilution techniques. Since there are

Table 1.

Cardiac Output Values in Standing Horses

Investigators	Cardiac output ml/kg/min
1. Fick principle	
Zuntz and Hagemann (1892)	75.0
2. Dye dilution technique	
Fisher and Dalton (1961)	75.0
Eberly, Gillespie and Tyler (1964)	90.0
Hall, Gillespie and Tyler (1968)	97.5
Eberly, Gillespie, Tyler and Fowler (1968)	82.7
Gillespie, Tyler and Hall (1969)	82.7
Kubo, Senta and Sugimoto (1973)	56.0
Bergsten (1974)	76.0
Hillidge and Lees (1975)	88.3 (ponies)
Muir, Skarda and Milne (1976)	73.9
3. Thermodilution Technique	
Muir, Skarda and Milne (1976)	72.2

many different types of thermodilution techniques and one had not been previously described for use in horses, five different volumes of injectate at two different temperatures were studied. Results obtained by injecting 40 ml of 0°C 5% dextrose in water into the right atrium were comparable to results obtained from the dye dilution studies (Table 1). Since the report of these results, other studies using the thermodilution technique for cardiac output determination have been done (Swanson, et al., 1985; Trim, et al., 1985). Today, only thermodilution and dye dilution methods are commonly used when measurement of cardiac output in horses is required.

2. Application of the Fick Principle for Estimation of Cardiac Output

In 1870, Adolf Fick (Wilson and Gibson, 1978) related cardiac output (CO), tissue oxygen consumption ($\dot{V}O_2$), and arteriovenous oxygen content difference ($A\text{-}VO_2$) in a formula, today known as the Fick principle.

$$CO = \frac{\dot{V}O_2}{A\text{-}VO_2}$$

The $A\text{-}VO_2$ will change inversely with CO when $\dot{V}O_2$ remains constant. Unless a patient is hypermetabolic, febrile, or in shock, $\dot{V}O_2$ will be approximately 145 ± 15 ml/min/m^2 (Wilson and Gibson, 1978). Therefore, $A\text{-}VO_2$ and variables determining this difference, such as mixed venous oxygen saturation ($S\bar{v}_{O_2}$) and mixed venous oxygen tension ($P\bar{v}_{O_2}$) have been used to

estimate CO or changes in CO. In the next section of this literature review, I will discuss the use of A-VO_2, $S\bar{V}_{O_2}$ and $P\bar{V}_{O_2}$ in the estimation of CO.

a. The Use of A-VO_2 Difference to Estimate CO

In a normal resting animal A-VO_2 is 4-5 ml O_2/100 ml blood. When CO does not meet the demand for O_2, this difference will increase to greater than 6 ml O_2/100 ml blood.

In 1978, Wilson et al reported results of a study that investigated the use of A-VO_2 difference to provide an estimate of cardiac output in 200 critical patients. Venous blood from the superior vena cava rather than true mixed venous blood from the pulmonary artery was used to measure the A-VO_2 difference. Cardiac output was measured using a dye dilution technique and was calculated using the measured A-VO_2 difference and an average $\dot{V}O_2$ of 135 ml/min/m^2. Calculated and measured cardiac indices were compared and calculated values were found to be approximately 23% higher than measured values. Although this difference was significant, there was a significant (r^2 = 0.49) correlation between the measured and calculated CI values. A-VO_2 difference and measured CI values were compared although no statistical analysis was done. There was an inverse relationship between A-VO_2 difference and CI. Patients with the lowest A-VO_2 differences had the highest CI values and patients with the highest A-VO_2 differences had the lowest CI values.

When measured CO and A-VO_2 difference were used to valculate $\dot{V}O_2$ and when $\dot{V}O_2$ was measured in 42 patients, the $\dot{V}O_2$ values were found to be quite variable. Values ranged from 63 ± 32 ml $O_2/min/m^2$ in one group to 158 ± 51 ml $O_2/min/m^2$ in another group.

Results from this paper suggest that there is an inverse relationship between A-VO_2 and CO, but whether A-VO_2 can be used to estimate CO is questionable. For any A-VO_2 there is a wide range of possible CO values associated with it. Variation in $\dot{V}O_2$ between patients contributes to the range of values. In patients such as these with cardiovascular instabilities and systemic disease, A-VO_2 cannot accurately and consistently reflect CO without simultaneous $\dot{V}O_2$ measurement.

b. The Use of $S\bar{V}_{O_2}$ to Estimate CO

Historically, as part of the method for Fick determination of cardiac output, $S\bar{V}_{O_2}$ has been recorded and noted to change as a function of CO. In a study of 36 critical patients, Cournand et al, in 1943, showed that $S\bar{V}_{O_2}$ decreased in proportion to the decrease in cardiac output. It wasn't until the late 1950's that monitoring $S\bar{V}_{O_2}$ was proposed as an alternative method for CO measurement. Various investigators studied the relationship between $S\bar{V}_{O_2}$ and CI or perfusion index in healthy subjects (Barratt-Boyes and Wood, 1957) and patients undergoing heart-lung bypass for cardiac defect repair (Moffitt et al, 1959, and Boyd et al,

1959). Each investigator noted the importance of $\dot{V}O_2$ and CaO_2 remaining constant or near constant in order for $S\bar{v}_{O_2}$ to accurately reflect the CO. An important point to note is that both healthy subjects and surgical patients on heart lung bypass have fairly stable respiratory and metabolic functions. This accounts for the predictable relationship the authors noted between $S\bar{v}_{O_2}$ and CO. Boyd et al actually separated his patients into two groups. Group 1 with cardiac index values above 2 L/min/m^2 and $S\bar{v}_{O_2}$ values above 50%, and group 2with CI and $S\bar{v}_{O_2}$ below 2 L/min/m^2 and 50%, respectively. There was a 66% mortality (10/15) in group 2 as compared to an 11% mortality (2/19) in group 1. This study (Boyd et al, 1959) demonstrated the importance of monitoring either CO or $S\bar{v}_{O_2}$ after open heart surgery to prevent the persistent low outflow state that precedes cardiac arrest.

As the use of $S\bar{v}_{O_2}$ to reflect CO became more common, physicians began recognizing the limitation of this relationship in critical patients with inadequate myocardial function (Valentine et al, 1966; Goldman et al, 1967; Goldman et al, 1968). In a majority of patients $S\bar{v}_{O_2}$ and CI were lowered but concurrent respiratory disease frequently interfered with the linear relationship between $S\bar{v}_{O_2}$ and CI that had previously been described in healthy patients. The monitoring of $S\bar{v}_{O_2}$ did not lose its importance at this time; rather, it began to be considered an important early indicator of the deterioration in oxygen delivery (Ca_{O_2} and CO) to the tissues. The patient's clinical course correlated with $S\bar{v}_{O_2}$, and changes

in $S\bar{v}O_2$ were shown to be early indicators of changes in clinical status or response to therapy (Goldman et al, 1967; Goldman et al, 1968; Kazarian and Del Guercio, 1980; de la Rocha et al, 1978).

In contrast to these results, Muir et al in 1970 described results of a study also designed to assess the use of $S\bar{v}O_2$ as a measurement of CO in patients with varying degrees of acute myocardial infarction. Indicator dilution measurements of CO were made in 26 patients. Mixed venous blood gas samples were taken just prior to determination of CO. Mixed venous oxygen tension was measured directly and $S\bar{v}O_2$ was derived from an oxyhemoglobin dissociation curve. There was a significant correlation ($r = 0.74$) between $S\bar{v}O_2$ and CI. In individual patients, changes in $S\bar{v}O_2$ appeared to correlate well with changes in CO. As was described in previous studies (Boyd et al, 1959; Goldman et al, 1968), $S\bar{v}O_2$ also appeared to relate to the clinical status of the patient. In order to explain the direct relationship between $S\bar{v}O_2$ and CO, Muir et al assumed that $\dot{V}O_2$ remained constant in patients with myocardial infarction even during low output states and that SaO_2 remained constant unless severe respiratory disease was present. These assumptions are acceptable in cases of uncomplicated myocardial infarction or left ventricular failure unless backward failure results in pulmonary edema. In cases where respiratory disease is present or $\dot{V}O_2$ is decreased as may occur in cases with backward failure and shock, other variables affecting $S\bar{v}O_2$ must be evaluated before attributing

the decrease in $S\bar{v}_{O_2}$ to inadequate CO alone (Hutter and Moss, 1970). The results of the study by Muir et al showed a large variation in the CI values for a given $S\bar{v}_{O_2}$ so a single measurement of $S\bar{v}_{O_2}$ was not shown to be useful in actual calculation of CO. As has been suggested by other investigators (Hutter and Moss, 1970; Lee et al, 1972), several measurements of $S\bar{v}_{O_2}$ would give a more accurate indication of changes in CO in response to therapeutic agents or due to depression of myocardial function, a decreased preload, or an increased afterload.

In 1978, de la Rocha et al published results of a study done in children and infants to determine the relationship between $S\bar{v}_{O_2}$ and cardiac index. Eleven patients undergoing surgery for congenital cardiac defects were monitored preoperatively, intraoperatively and postoperatively. Variables monitored included $S\bar{v}_{O_2}$, cardiac index and various systemic, pulmonary and cardiac pressures. Linear regression analysis was done to evaluate the relationship between $S\bar{v}_{O_2}$ and cardiac index. A significant correlation was found ($r = 0.78, p < .001$). All $S\bar{v}_{O_2}$ values less than 65% corresponded to a cardiac index of less than 2.5 L/min/m^2 except in one case. Patients with low cardiac output syndromes postoperatively (n=3) were treated with positive inotropes. This resulted in an increase in both $S\bar{v}_{O_2}$ and cardiac index ($r = 0.86, p < .05$). Patients with uncomplicated recoveries had $S\bar{v}_{O_2}$ values greater than 65% and normal cardiac index values. The one exception to this was a patient with a normal cardiac index with a $S\bar{v}_{O_2}$ lower than 65%. This

patient was also pyrexic. Oxygen consumption increases 10-13% for each degree Celsius elevation in body temperature above 37°C and may be responsible in this case for lowering $S\bar{v}O_2$.

This study confirmed a significant correlation between cardiac index and $S\bar{v}O_2$. These results supported the results of studies by Moffitt et al and Boyd et al in 1959 showing that surgical patients appeared to be good cases to use $S\bar{v}O_2$ for evaluation of CO. Generally, their metabolic rate is stable which minimizes problems due to changing $\dot{V}O_2$. This is in contrast to septic shock patients where higher metabolic rates and lower $\dot{V}O_2$ occurs resulting in a decreased A-VO_2 (Duff et al, 1969). Despite the significant relationship between CI and $S\bar{v}O_2$, a specific $S\bar{v}O_2$ measurement had a range of CI values associated with it and an increase of $S\bar{v}O_2$ less than 10% did not associate well with a similar rise in CI (de la Rocha, 1978). The results of this study suggest that an $S\bar{v}O_2$ value less than 65% warrants further investigation and in surgical patients with no preexisting metabolic or respiratory disease emphasis can be placed on the patient's cardiovascular function.

Investigations between 1959 and 1970 of the use of $S\bar{v}O_2$ as an indicator of cardiac output confronted the following problems which precluded its wide acceptance into postoperative and critical care. (1) Single $S\bar{v}O_2$ measurements were difficult to interpret because of the large variability in cardiac index values for a specific $S\bar{v}O_2$. (2) Changes in

cardiac output and $S\bar{v}_{O_2}$ occurred rapidly, and single or intermittent measurements were not adequate for monitoring of unstable patients. (3) The number of samples taken could be influenced by patient blood volume and hemoglobin concentration and (4) in vitro measurement of these samples was time consuming.

The first report of continuous $S\bar{v}_{O_2}$ measurement was made in 1962 by McArthur et al. This study described the use of a system whereby small amounts of mixed venous blood (18 ml blood/hour) were pumped continuously from the pulmonary artery to an anaerobic mixing cuvette equipped with an oxygen electrode for measurement of $S\bar{v}_{O_2}$. It wasn't until 1972 that a method for continuous in vivo measurement of $S\bar{v}_{O_2}$ was described. This technique involved the use of a fiberoptic catheter oximeter which used alternating pulses of light at either 670 and 950 or 660 and 805 nm wavelengths. Reflected light was transmitted by a second set of fibers to a photoelectric device outside the patient. The ratio of intensities of the back scattered light of the two wavelengths was used to determine oxygen saturation. Investigators (Martin et al, 1973) showed a significant correlation ($r = 0.978$) between simultaneously measured in vitro oximeter and fiberoptic oximeter $S\bar{v}_{O_2}$ values.

In 1975 Krauss et al reported results of a study describing the use of this catheter to measure $S\bar{v}_{O_2}$ in patients after cardiothoracic surgery. The intent of this project was to determine the predictive value of $S\bar{v}_{O_2}$ during

the postoperative period after thoracotomy. The value of $S\bar{V}O_2$ as a predictor of cardiac output was also investigated. Fiberoptic catheters for continuous $S\bar{V}O_2$ measurement were placed in 19 patients either prior to (12) or after (7) surgery. Other variables monitored were cardiac index, arterial blood gases and pH, systemic and various cardiac pressures, and urine production. A correlation was found between cardiac index and $S\bar{V}O_2$ ($r = 0.78$, $n = 28$, $0.64 < p < 0.92$) but only if $S\bar{V}O_2$ were stable (change in $S\bar{V}O_2$ of <3%) for at least five minutes before and after the measurement of CI. When CI was less than 2.0 L/min/m^2, $S\bar{V}O_2$ was less than 60% in six out of eight patients. When CI was less than 2.5 L/min/m^2, all but one patient had an $S\bar{V}O_2$ less than 65%. Urine production less than 20 ml/min, systemic blood pressure under 90/60 mmHg or other clinical signs of shock were preceded by a fall in $S\bar{V}O_2$ of more than 5% or to values less than 60%. In patients that experienced respiratory distress, there was a simultaneous fall in $S\bar{V}O_2$.

The results of this study support the contention that a changing $S\bar{V}O_2$ reflects changes in variables determining this value, namely cardiac output, SaO_2, hemoglobin and $\dot{V}O_2$. Trying to evaluate $S\bar{V}O_2$ as an indicator of CO is impossible in patients with potential for respiratory dysfunction or metabolic instabilities. $S\bar{V}O_2$ was shown in this study to change prior to obvious changes in other monitoring variables such as heart rate and blood pressure. Because of this, it may be useful as an early indicator of cardiovascular or

respiratory dysfunction. This study supported the use of continuous monitoring of $S\bar{v}O_2$ as a valuable monitoring tool in the care of critical postsurgical patients. These conclusions were corroborated by results of similar studies by Martin et al, 1973, and McArthur et al, 1962.

In 1978, a new system for reflection spectrophotometry was developed using light pulses of three different wavelengths between 600 and 1000 nm (Wilkinson et al, 1979). Reflected light is transmitted to a photodetector to measure blood reflectance and to compute $S\bar{v}O_2$ from the relative intensities corresponding to the three different wave lengths. A digital readout shows the average value for the preceding five seconds and is updated every second. Although it is more difficult to use (Schmidt and Staff, 1981), this catheter is more accurate than the older one because three different light wavelengths are used.

In 1982, Jamieson et al used this fiberoptic catheter to compare hemodynamic parameters with $S\bar{v}O_2$ in eighty-four patients at six predetermined periods between preparation for induction and recovery. Hemodynamic assessment included measurement of heart rate, arterial blood gases, systemic blood pressure, right atrial (CVP), left atrial (LAP) and pulmonary capillary wedge (PCWP) pressures, temperature and cardiac output. Calculations of cardiac index, systemic (SVR) and pulmonary (PVR) vascular resistances and left ventricular stroke work index were then done. Observations were made in the postoperative period to assess effects of endotracheal

tube suctioning, positioning, shivering, and chest physiotherapy on the measured variables. During surgery a decreased $S\bar{v}_{O_2}$ was treated with inotropic agents and vasopressors or vasodilators. Interpretation of therapeutic needs based on $S\bar{v}_{O_2}$ correlated well with other hemodynamic measurements. Changes in $S\bar{v}_{O_2}$ of more than 10% often preceded changes in the hemodynamic status of the patient. When $S\bar{v}_{O_2}$ began to fall, the patient was evaluated for a decrease in preload (CVP, PCWP, LAP), contractility (LV stroke index) and an increase in afterload (SVR, PVR) and treated appropriately until $S\bar{v}_{O_2}$ improved. Shivering, endotracheal tube suctioning, position changes and chest physiotherapy markedly decreased $S\bar{v}_{O_2}$. $S\bar{v}_{O_2}$ improved when manipulation of the patient and/or shivering ceased.

This study confirmed the importance of $S\bar{v}_{O_2}$ as an early indicator of adequate tissue perfusion. In patients with stable $\dot{V}O_2$, hemoglobin concentration and respiratory function, $S\bar{v}_{O_2}$ was also used to estimate cardiac output but $S\bar{v}_{O_2}$ and cardiac output had no "fixed" relationship.

In 1982, two studies evaluating technical problems associated with placement of a new fiberoptic catheter were published. This catheter had both fiberoptic $S\bar{v}_{O_2}$ measurement capabilities and the capacity for thermodilution cardiac output measurement. The study by Baele et al used critically ill adult patients requiring hemodynamic monitoring. Waller et al placed these catheters in patients undergoing cardiac surgery. Measurements made included

in vivo fiberoptic measurement of $S\bar{v}_{O_2}$, in vitro oximeter measurement of $S\bar{v}_{O_2}$, and cardiac output. Patients in both studies were breathing an oxygen enriched gas. Baele et al found a significant correlation between in vitro and in vivo measurement of $S\bar{v}_{O_2}$ ($r = 0.95$). Waller et al found the correlation to be significant as well ($r = 0.92$, $n = 99$). This was true for a range of $S\bar{v}_{O_2}$ values from 60-95% measured with hemotocrits of 20-42%.

Waller et al found a significant correlation between $S\bar{v}_{O_2}$ and hemodynamic changes. An increase or decrease in $S\bar{v}_{O_2}$ >5% correlated with a change in cardiac index ($r = 0.69$), stroke index ($r = 0.67$), and left ventricular stroke work index ($r = 0.58$). There were 39 instances when $S\bar{v}_{O_2}$ values changed by 5% or more. Eighteen of 21 decreases in $S\bar{v}_{O_2}$ were accompanied by corresponding decreases in cardiac index and 14 of 18 $S\bar{v}_{O_2}$ increases were accompanied by an increase in cardiac index. In vivo $S\bar{v}_{O_2}$ values did not correlate significantly with changes in mean arterial pressure, heart rate, pulmonary capillary wedge pressure or systemic vascular resistance. Baele et al showed by multivariant analysis that hemoglobin concentration, body temperature and cardiac index did not affect the accuracy of in vivo $S\bar{v}_{O_2}$ measurement.

Both of these studies support the hypothesis that $S\bar{v}_{O_2}$ can be determined accurately in vivo by fiberoptic catheter measurement. $S\bar{v}_{O_2}$ correlated with CO but the relationship was not strong enough to define actual cardiac output values from $S\bar{v}_{O_2}$ measurement. However, if $S\bar{v}_{O_2}$ did decrease by 5%

or more, Waller et al showed there was an 86% chance that cardiac index had also decreased. Because $S\bar{v}_{O_2}$ is continuously measured and cardiac output is not, $S\bar{v}_{O_2}$ can serve as an early indicator of a diminished cardiac output. $S\bar{v}_{O_2}$ also reflects changes in other important variables and may be more useful than any one of the other variables that determine $S\bar{v}_{O_2}$ in critical patient care.

A more recent study using the fiberoptic continuous $S\bar{v}_{O_2}$ measurement was by Schmidt et al, 1984. This study compared continuous $S\bar{v}_{O_2}$ measurement with intermittently measured and calculated oxygen transport variables in the preoperative period of twenty adult cardiac surgery patients. All of these patients had impaired left ventricular function. Measurements made included continuous $S\bar{v}_{O_2}$, systemic blood pressure, cardiac filling pressures and heart rate. Intermittent arterial blood gases and cardiac output measurements were made. Calculations included A-VO_2, oxygen delivery ($\dot{D}O_2 = CO \times CaO_2$), $\dot{V}O_2$ and oxygen extraction ratio (OER = $\dot{V}O_2/\dot{D}O_2$). There was a significant negative correlation ($r = -0.84$) between $S\bar{v}_{O_2}$ and percentage of O_2 extracted from the blood (OER). No other oxygen transport variables including cardiac index showed significant correlation with $S\bar{v}_{O_2}$. Changes in $S\bar{v}_{O_2}$ on occasion preceded changes in cardiac output but there was a large variation in the amount of change. At the onset of anesthesia, $S\bar{v}_{O_2}$ actually increased 15% and cardiac output decreased.

As was described by Schmidt et al, the relationship of $S\bar{V}_{O_2}$ to OER is more obvious if the equation $OER = \dot{V}O_2/\dot{D}O_2$ is simplified

$$OER = \frac{CO\ (CaO_2 - C\bar{V}_{O_2})}{CO \times CaO_2}$$

$$OER = 1 - \frac{C\bar{V}_{O_2}}{CaO_2}$$

since the majority of the oxygen in whole blood is bound to hemoglobin CaO_2 and $C\bar{V}_{O_2}$ can be simplified to SaO_2 and $S\bar{V}_{O_2}$. SaO_2 is usually about 100%, so

$$OER = 1 - S\bar{V}_{O_2}$$

Using $S\bar{V}_{O_2}$ to estimate OER is less variable than using $S\bar{V}_{O_2}$ to estimate CO and OER is more significant than CO in assessing tissue oxygenation. In a patient with normal $\dot{V}O_2$ a decrease in CO can cause a decreased $S\bar{V}_{O_2}$. When $\dot{V}O_2$ increases and CO remains constant, $S\bar{V}_{O_2}$ will also decrease. Schmidt et al claim that the cause of the decrease in $S\bar{V}_{O_2}$ is not as important as the level to which it decreases. Arterial hypoxemia is just as significant a cause of tissue hypoxia as is a decreased CO. It is difficult to use $S\bar{V}_{O_2}$ as an estimate of CO since a multifactorial relationship exists. Other variables ($\dot{V}O_2$ and SaO_2) involved in this relationship may change at any time in critical care patients. Actual CO is not as relevant in patient care as is adequate tissue oxygenation. The reason emphasis is placed on maintaining or increasing CO is to assure tissues have enough oxygen to survive. The Fick Principle has been used widely in the past

to estimate cardiac output because CO has been so difficult to measure. Rapid changes in CO are difficult to detect because indicator dilution measurement of CO has time and indicator volume limits. If $S\bar{v}_{O_2}$ were difficult to measure and CO was easy, CO measurement would likely be investigated as a way to estimate $S\bar{v}_{O_2}$. $S\bar{v}_{O_2}$ reflects significant changes in CO, $\dot{V}O_2$ and arterial oxygenation and is an extremely useful monitoring variable in critical patient care.

The purpose of $S\bar{v}_{O_2}$ monitoring has evolved over the last 30 years. Initially it was monitored to reflect CO, a value rarely measured clinically because indicator dilution techniques were difficult to apply. Today $S\bar{v}_{O_2}$ is thought of as a variable which if monitored continuously will reflect early changes in a patient's tissue oxygenation which is a function of CO, systemic vascular resistance, pulmonary gas exchange and hemoglobin concentration. $S\bar{v}_{O_2}$ is believed to be more sensitive and a better prognostic indicator than any other single variable monitored in critical care patients (Schmidt et al, 1984). $S\bar{v}_{O_2}$ is also still useful in estimation of CO in patients with stable respiratory and metabolic functions (Sottile et al, 1982; Magilligan et al, 1983; Sheldon et al, 1983).

c. The Use of $P\bar{v}_{O_2}$ to Estimate CO

One other way to evaluate CO is by $P\bar{v}_{O_2}$ measurement. $P\bar{v}_{O_2}$ is an indicator of tissue oxygenation and describes the

driving force moving oxygen from the blood to the tissues. Diffusion of oxygen is entirely dependent on P_{O_2} and not on the total amount of oxygen present. The speed and distance over which diffusion occurs depends on a partial pressure gradient. Oxygen dissociates from hemoglobin based on the binding affinity of hemoglobin for oxygen. This affinity is described by the oxyhemoglobin dissociation curve. Carbon dioxide tension, pH, temperature and concentration of 2,3 DPG inside the red blood cell determine the slope of this curve. At a P_{O_2} of 40 mmHg approximately 75% of the hemoglobin is bound. Between a P_{O_2} of 70 and 20 mmHg, there is a linear relationship between S_{O_2} and P_{O_2}. Over this portion of the curve P_{O_2} determines S_{O_2}. $P\bar{v}_{O_2}$ is usually maintained between 36-40 mmHg. If this value decreases below 30 mmHg compensatory mechanisms come into play. These mechanisms include a release of catecholamines which increase CO and $P\bar{v}_{O_2}$. When $P\bar{v}_{O_2}$ decreases it is because the circulatory system is failing to keep pace with the tissues' oxygen demands (Miller, 1982; Finch and Lenfant, 1972; Snyder and Carroll, 1982).

The first investigators to propose that $P\bar{v}_{O_2}$ was a useful indicator of the adequacy of tissue blood flow was Stanley and Isern-Amaral in 1974. Their conclusion was supported only by the fact that in patients where $P\bar{v}_{O_2}$ was kept between 38-42 mmHg during bypass there was a significantly greater urine output and significantly lower bicarbonate requirements than in patients perfused at a

fixed rate of 40-60 ml/kg/min. Statistical evidence to support the use of $P\bar{v}_{O_2}$ in estimation of CO was provided later by Parr et al in 1975 and Kohanna et al in 1981. In a study of 139 children less than two years of age and after cardiac surgery, Parr et al showed that there was a statistically significant correlation between CI and $P\bar{v}_{O_2}$. The results also showed that acute cardiac death was more reliably predicted using CI and $P\bar{v}_{O_2}$ than either one alone.

Kohanna et al also discussed results supporting a statistically significant correlation between $P\bar{v}_{O_2}$ and CI. This was shown in a study of 25 patients after cardiac operations. The thermodilution CO measurements were made and compared to $P\bar{v}_{O_2}$, Pa_{O_2}, $P\bar{v}_{CO_2}$, Pa_{CO_2}, venous and arterial pH, packed red cell volume, temperature, left atrial pressure, central venous pressure, urine output, heart rate, and mean arterial pressure. Only $P\bar{v}_{O_2}$, $P\bar{v}_{CO_2}$, Pa_{CO_2}, venous and arterial pH, and temperature had significant r values ($p < 0.01$) and the highest r value was found with the correlation between CI and $P\bar{v}_{O_2}$ ($r = 0.49$). The authors (Kohanna et al and Parr et al) state that the correlation between $P\bar{v}_{O_2}$ and CI were too low to be relied on clinically and that measurement of CO was the only accurate way to determine adequate cardiac function. As an alternate use for $P\bar{v}_{O_2}$ Kasnitz et al evaluated its use as a prognostic indicator for critically ill patients with circulatory and/or respiratory abnormalities. Results of the study showed that all of the nine patients with $P\bar{v}_{O_2}$ values less than

28 mmHg died, whereas only two of the eleven patients with $P\bar{v}O_2$ values greater than 28 mmHg died. They also showed that measurement of $P\bar{v}O_2$ alone was a better prognostic indicator than measurement of CO alone in critically ill patients.

By 1978, continuous monitoring of $S\bar{v}O_2$ had been reported and shown to be superior to intermittent $S\bar{v}O_2$ monitoring. In an effort to apply this technique to $P\bar{v}O_2$ monitoring, Armstrong et al described the use of continuous $P\bar{v}O_2$ measurement in monitoring twenty-five patients with cardiorespiratory disorders. A double lumen catheter was used with a miniature polarographic electrode mounted on the end. During periods of cardiorespiratory stability, the mean $P\bar{v}O_2$ was 43,4 ± 0.3 mmHg. Decreases in $P\bar{v}O_2$ below 40 mmHg occurred in patients experiencing a reduction in F_IO_2, acute respiratory failure, hypoventilation, hypovolemia and cardiac arrhythmias. In four of five cases, the decrease in $P\bar{v}O_2$ preceded clinical signs of deterioration.

It is clear from the results discussed that $P\bar{v}O_2$ cannot be used for estimation of CO in patients with unstable respiratory or metabolic function. When respiratory and metabolic function are stable, then, as was demonstrated with $S\bar{v}O_2$ (Scottile et al, Magilligan et al, Sheldon et al, Boyd et al), $P\bar{v}O_2$ is useful for estimation of CO.

As pointed out earlier, a decrease in CO is a common cause of life threatening complications in horses. Because

metabolic and respiratory function are likely to be stable in anesthetized horses, I hypothesized that $P\bar{v}_{O_2}$ is a useful indicator of CO in anesthetized horses. Furthermore, in order to enhance the clinical applicability of this research, the relationship between $P\bar{v}_{O_2}$ and CO was studied with horses in dorsal, lateral, and sternal recumbencies and in horses with a metabolic disturbance induced by Escherichia coli endotoxin administration.

MATERIALS AND METHODS

Horses - Six healthy mixed breed horses (9.8 ± 3.6 years of age, weighing 466.2 ± 18.5 kg [$\bar{x}$ ± SEM]) were used.

Measurement techniques - For measurement of CO, a 110-cm 7-F balloon-tipped catheter with a thermistor near the tip[a] was percutaneously placed in the pulmonary artery via the jugular vein. A polyethylene catheter (inside diameter 1.67 mm, outside diameter 2.42 mm)[b] was percutaneously placed in the right atrium also via the jugular vein. Catheters were attached to pressure transducers,[c] and an oscilloscope[d] was used to verify placement by the presence of characteristic pressures and wave form. The zero pressure reference point was considered to be at the level of the sternum for horses in lateral recumbency and at the point of the shoulder for horses in sternal and dorsal recumbency. To measure CO, 40 ml of 0°C 5% dextrose in water was injected in <2 s into the right atrium using a pressure injector[e] at 27.2 atmospheres. Falsely increased CO data were obtained when indicator solution was allowed to warm in the atrial catheter before making CO measurements. To prevent this, the atrial catheter was filled with cold 5% dextrose in water just before CO measurement. Injections of indicator solution were made during exhalation at the onset of a QRS

complex. Cardiac output was calculated using a CO computer.[a] Each data point was the mean of at least three CO determinations.

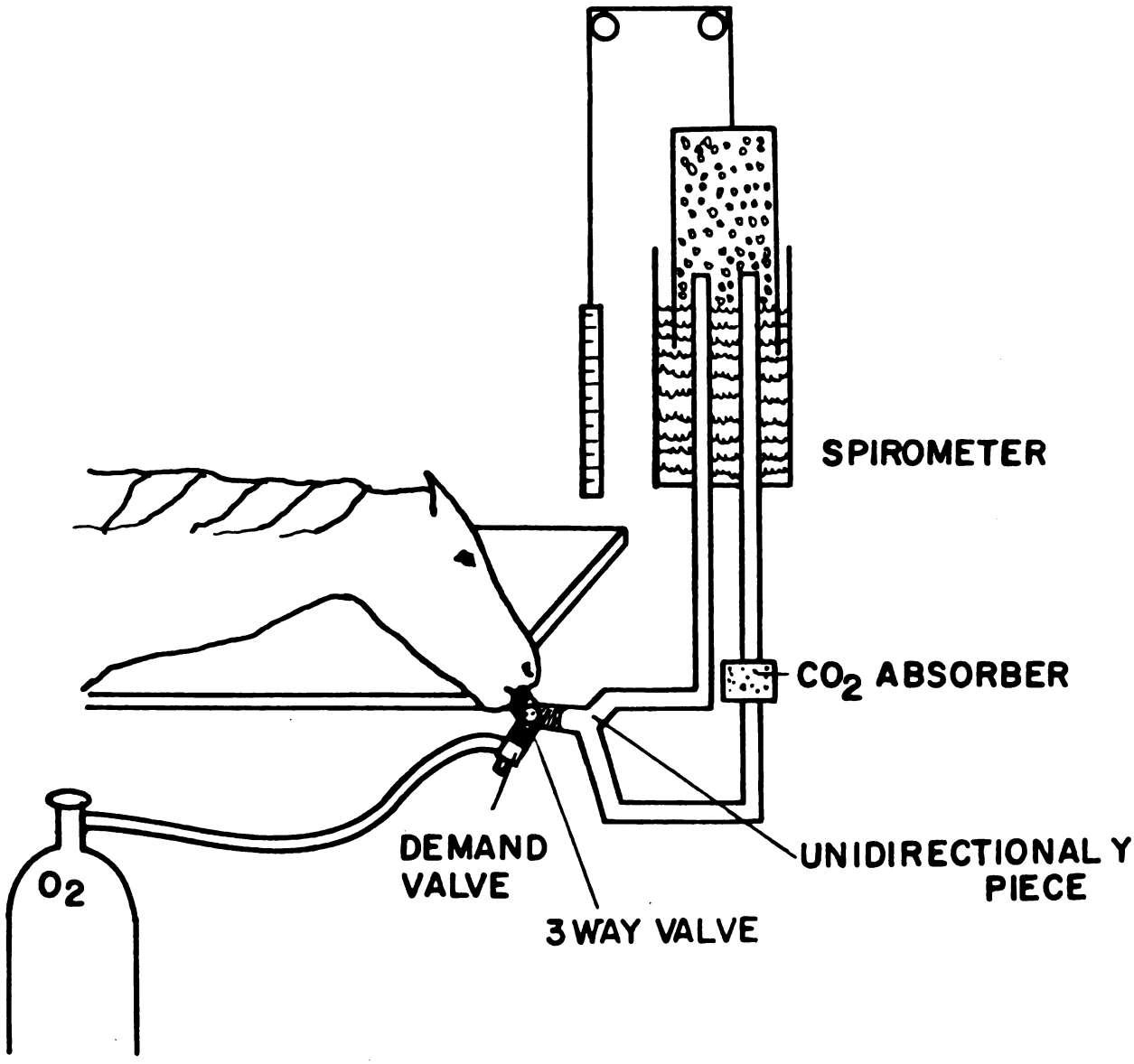
Oxygen consumption was measured volumetrically (Brody, 1945). Briefly, at end exhalation, the endotracheal tube[f] was connected through a three-way valve[g] to a 120-L spirometer[g] containing a known volume of 100% O_2 (Figure 1). The horse was allowed to breathe from the spirometer through a unidirectional Y piece for five minutes. Carbon dioxide was removed from the circle system using a CO_2 absorbant.[h] At the end of exhalation after approximately five minutes of breathing through the spirometer, the three-way valve was switched to allow the horse to breathe through the demand valve.[i] The change in gas volume in the spirometer was measured, and a calculation of $\dot{V}O_2$ was made. Values were corrected to STPD using standard equations.

Blood samples were collected anaerobically from the facial artery, pulmonary artery, jugular vein, and a superficial limb vein (median or medial saphenous). Blood gas tensions were determined using a blood gas analyzer.[j] Mean arterial blood pressure was measured using a facial artery catheter[k] and pressure transducer connected to a multichannel physiograph. Heart rate was measured using a bipolar ECG lead system.[d] From these values we calculated stroke volume (SV), (SV = CO/HR) and peripheral vascular resistance (PVR)

$$PVR = MAP/CO$$

Figure 1.

Equipment used for measurement of oxygen consumption.


SPIROMETER
CO_2 ABSORBER
DEMAND VALVE
UNIDIRECTIONAL Y PIECE
3 WAY VALVE
O_2

where MAP is mean arterial blood pressure. Cardiac index was calculated using the equations (Henness et al, 1977)

$$CI = CO/\text{body surface area}$$

where

$$\text{body surface area } (m^2) = (10.1 \times W^{2/3})/10^4$$

and W is body weight in grams.

Experimental design - Horses were fasted for 12 hours before anesthetic induction. After placement of catheters in the pulmonary artery, right atrium and jugular vein, anesthesia was induced with 1 mg of xylazine[l]/kg of body weight IV and 2 mg of ketamine[m]/kg, IV. A surgical anesthetic plane was maintained with a mixture of 10% guaifenesin[n] and 0.4% thiamylal[o] for 4.4 ± 0.1 hours. Horses ventilated spontaneously through an endotracheal tube and a demand valve that delivered 100% O_2. Horses were placed in lateral, sternal, or dorsal recumbency as predetermined by two 3 x 3 latin square designs (Table 2). To achieve a low CO, xylazine (0.65 to 1 mg/kg, IV) was administered. At least five minutes after xylazine administration, CO and then $\dot{V}O_2$ were measured. During the $\dot{V}O_2$ measurement, blood samples were taken for O_2 and CO_2 tension measurements. Heart rate (HR) and MAP were also recorded during the $\dot{V}O_2$ measurement period. Subsequently, to increase CO, dobutamine[p] in 5% dextrose and water was administered by an infusion pump[q] at 1 to 7 µg/kg/min. In four instances during dobutamine administration, a persistent second degree atrioventricular (AV) block was observed. Because this arrhythmia

Table 2.

3 x 3 latin square design describing random sequencing of recumbencies.

Recumbencies		
First	Second	Third
Lateral	Sternal	Dorsal
Lateral	Dorsal	Sternal
Sternal	Dorsal	Lateral
Sternal	Lateral	Dorsal
Dorsal	Lateral	Sternal
Dorsal	Sternal	Lateral

interferes with indicator dilution CO measurement, 3 to 5 mg of atropine sulfate was administered IV. After at least five minutes of dobutamine administration, all measurements were repeated in the sequence described. The horse was then moved to the next position, and the series of measurements was repeated as described. Steady state was determined throughout each measurement period by constant monitoring of MAP and HR. Repeated measurements of CO and $\dot{V}O_2$ were made periodically at the end of the measurement periods and were never significantly different from earlier CO and $\dot{V}O_2$ measurements made during that period.

To determine if the relationship between CO and $P\bar{v}_{O_2}$ applied to horses with endotoxemia, horses were placed in dorsal recumbency after the last measurement period and Escherichia coli endotoxin[r] was administered. An endotoxin dose of 100 μg/kg was suspended in 60 ml of 0.9% NaCl and was administered IV over a period of five minutes. Fifteen minutes after endotoxin administration, measurements were repeated.

Statistical analysis - The effect of position on all variables was analyzed using a two-way analysis of variance. If a significant F value were found, Tukey's ω test was used to compare means. The effect of dobutamine and endotoxin administration was analyzed using paired *t* tests. Linear regression analysis was used to relate CI and $P\bar{v}_{O_2}$, HR, MAP, jugular venous oxygen tension (Pv_{O_2} JUG) and superficial limb

vein O_2 tension (P_{VO_2} PERIPH). Significance was determined by calculation of a *t* value for the regression coefficient (b). Significance was set at $P < 0.05$.

RESULTS

Positioning had an effect on CO, CI, SV, PVR, MAP, and Pa_{O_2} (Table 3). When compared with values in horses in lateral recumbency, after xylazine administration, CO, CI and SV were lower in horses in sternal recumbency whereas PVR was higher in horses in sternal recumbency. In horses in dorsal recumbency, after xylazine administration, MAP, PVR and Pa_{O_2} were significantly lower and CO and CI were significantly higher than those in horses in sternal recumbency but not those in horses in lateral recumbency.

In horses in all positions, dobutamine increased CO, CI, HR, MAP, $P\bar{v}_{O_2}$, Pv_{O_2} JUG, and Pv_{O_2} PERIPH (Table 3) but the increase in HR was not significant in horses in lateral recumbency. Dobutamine also increased $\dot{V}O_2$ but the increase was only significant in horses in sternal recumbency. In horses in sternal recumbency, dobutamine increased SV and decreased PVR. In horses in dorsal recumbency, dobutamine significantly increased Pa_{O_2}. In horses in lateral recumbency, dobutamine significantly increased Pa_{CO_2}.

When compared with data obtained after xylazine administration with horses in dorsal recumbency, endotoxin administration increased HR and decreased SV and Pv_{O_2} PERIPH. Other variables were not changed significantly.

Table 3.

Cardiovascular measurements after xylazine (0.65 to 1 mg/kg) and after dobutamine administration (1 to 7 µg/kg/min) and 15 minutes after endotoxin administration (100 µg/kg) in six anesthetized horses.

Measurement	Lateral		Sternal		Dorsal		
	Xylazine	Dobutamine	Xylazine	Dobutamine	Xylazine	Dobutamine	Endotoxin
CO (ml/kg/min)	64.0 ± 4.3	95.9 ± 12.5*	39.1 ± 5.1†♦	91.0 ± 13.3*	60.5 ± 5.6	94.4 ± 12.2*	59.5 ± 7.3
CI (L/min/m^2)	4.90 ± 0.34	7.36 ± 0.94*	3.00 ± 0.40†♦	7.00 ± 1.06*	4.64 ± 0.45	7.22 ± 0.94*	4.59 ± 0.60
SV (ml)	830.0 ± 114.2	889.1 ± 62.4	546.2 ± 75.0†	804.8 ± 94.2*	747.5 ± 82.7	811.3 ± 107.2	488.2 ± 55.8*
HR (beats/min)	37.7 ± 2.9	60.3 ± 11.4	33.7 ± 2.1	53.8 ± 6.9*	38.8 ± 3.3	56.5 ± 7.5*	57.7 ± 4.9*
MAP (mm of Hg)	82.7 ± 6.5	138.0 ± 11.8*	114.5 ± 7.4♦	159.5 ± 3.8*	72.0 ± 7.0	128.3 ± 11.5*	90.3 ± 16.6
PVR (mm of Hg/L/min)	2.84 ± 0.29	3.29 ± 0.36	7.29 ± 1.69†♦	4.39 ± 0.87*	2.65 ± 0.30	3.07 ± 0.29	3.31 ± 0.45
$\dot{V}O_2$ (ml/kg/min)	1.78 ± 0.13	2.11 ± 0.20	1.84 ± 0.10	2.32 ± 0.21*	1.89 ± 0.17	2.20 ± 0.12	1.65 ± 0.18
Pa_{O_2} (mm of Hg)	266.5 ± 36.0	266.3 ± 20.1	343.4 ± 24.8♦	374.0 ± 14.9	170.6 ± 26.1	232.9 ± 14.3*	143.5 ± 36.1
$P\bar{v}_{O_2}$ (mm of Hg)	49.9 ± 2.2	69.6 ± 4.1*	48.9 ± 2.5	97.0 ± 13.6*	45.3 ± 1.2	69.8 ± 3.7*	43.9 ± 2.8
Pa_{CO_2} (mm of Hg)	54.5 ± 1.4	57.4 ± 1.2*	53.0 ± 4.2	56.6 ± 2.5	60.5 ± 4.2	61.3 ± 2.9	52.5 ± 4.0
Pv_{O_2} PERIPH (mm of Hg)	102.3 ± 25.8	130.9 ± 26.6*	55.6 ± 2.2	128.0 ± 15.0*	50.3 ± 5.0	80.9 ± 12.3*	39.8 ± 5.1*
Pv_{O_2} JUG (mm of Hg)	57.0 ± 3.4	78.2 ± 6.6*	56.6 ± 5.8	116.5 ± 22.4*	53.9 ± 3.3	87.2 ± 7.0*	50.5 ± 4.4

CO = cardiac output; CI = cardiac index; SV = stroke volume; HR = heart rate; MAP = mean arterial blood pressure; PVR = peripheral vascular resistance; $\dot{V}O_2$ = O_2 consumption; Pa_{O_2} = arterial O_2 tension; $P\bar{v}_{O_2}$ = mixed venous O_2 tension; Pa_{CO_2} = arterial CO_2 tension; Pv_{O_2} PERIPH = superficial limb venous O_2 tension; Pv_{O_2} JUG = jugular venous O_2 tension.

* = Significantly different ($P < 0.05$) from xylazine data.

† = Significantly different ($P < 0.05$) from lateral recumbency after xylazine administration.

♦ = Significantly different ($P < 0.05$) from dorsal recumbency after xylazine administration.

Correlations between CI and HR, MAP, $P\bar{v}_{O_2}$, Pv_{O_2} JUG, and Pv_{O_2} PERIPH were statistically significant (Figures 2-6, Tables 4 and 5). There was a significant relationship between CI and either $P\bar{v}_{O_2}$ or MAP in all positions and after endotoxin administration. In horses in sternal recumbency, Pv_{O_2} JUG and Pv_{O_2} PERIPH did not significantly correlate with CI. In horses in lateral recumbency, the correlation between Pv_{O_2} PERIPH and CI was also not significant. There was a significant correlation between HR and CI in horses in all positions, but not after endotoxin administration (Table 5).

Figure 2.

The relationship between mixed venous O_2 tension ($P\bar{v}_{O_2}$) and cardiac index (CI). Measurements made in six horses in lateral, sternal, and dorsal recumbencies and in dorsal recumbency after endotoxin administration are shown on upper panels; cumulative data are shown in lower panel. Regression coefficient (b) ± SE of the regression coefficient. All b and R values are significant. (Δ = xylazine, O = dobutamine, □ = endotoxin.)

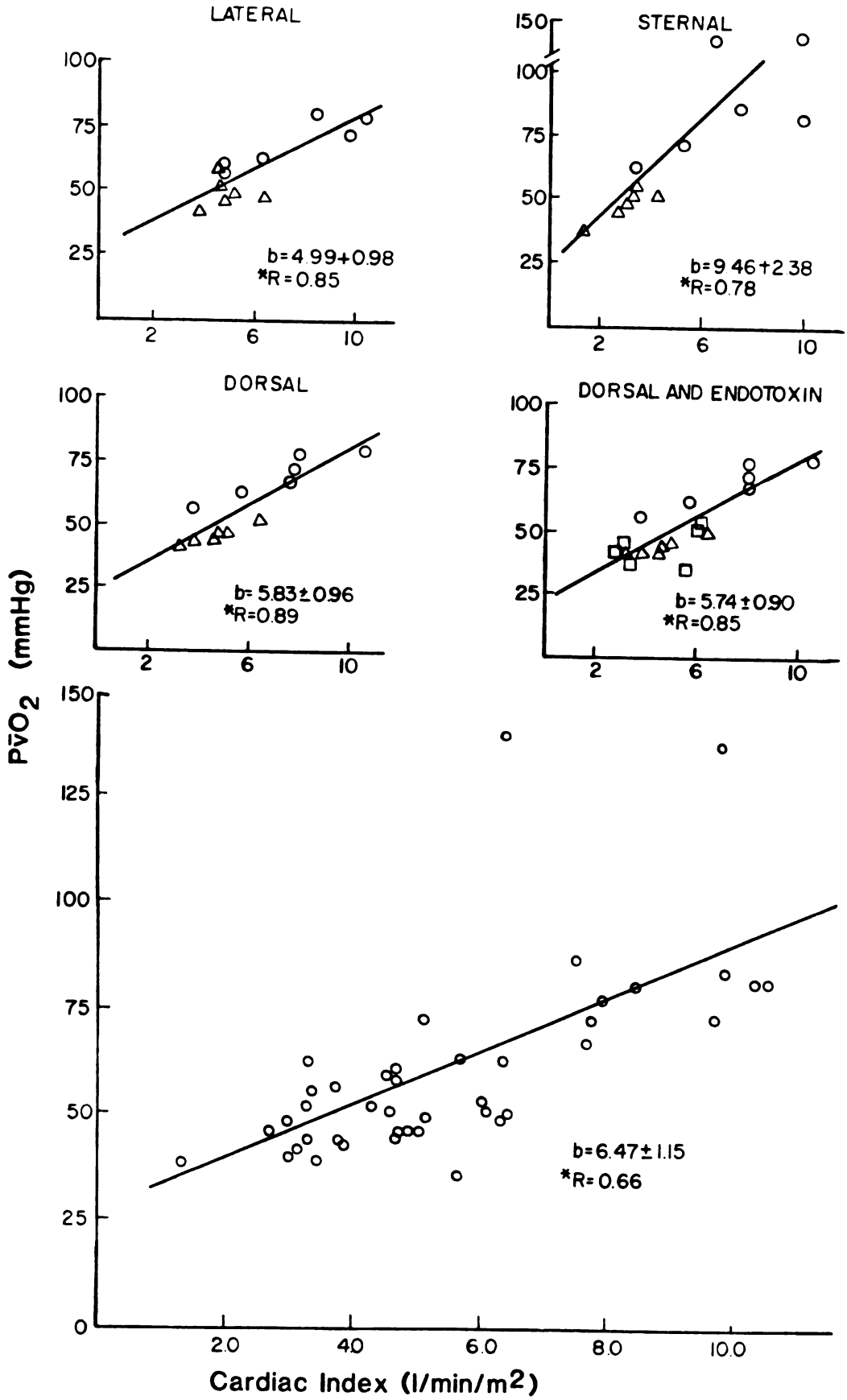

LATERAL
b=4.99+0.98
*R=0.85
STERNAL
b=9.46+2.38
*R=0.78
DORSAL
b=5.83±0.96
*R=0.89
DORSAL AND ENDOTOXIN
b=5.74±0.90
*R=0.85
b=6.47±1.15
*R=0.66
PvO2 (mmHg)
Cardiac Index (l/min/m2)

Figure 3.

The relationship between jugular venous O_2 tension (Pv_{O_2} JUG) and cardiac index (CI). Measurements made in six horses in lateral, sternal, and dorsal recumbencies and in dorsal recumbency after endotoxin administration are shown on upper panels; cumulative data are shown in lower panel. Regression coefficient (b) ± SE of the regression coefficient. Significant b and R values are indicated (*). (Δ = xylazine, O = dobutamine, □ = endotoxin.)

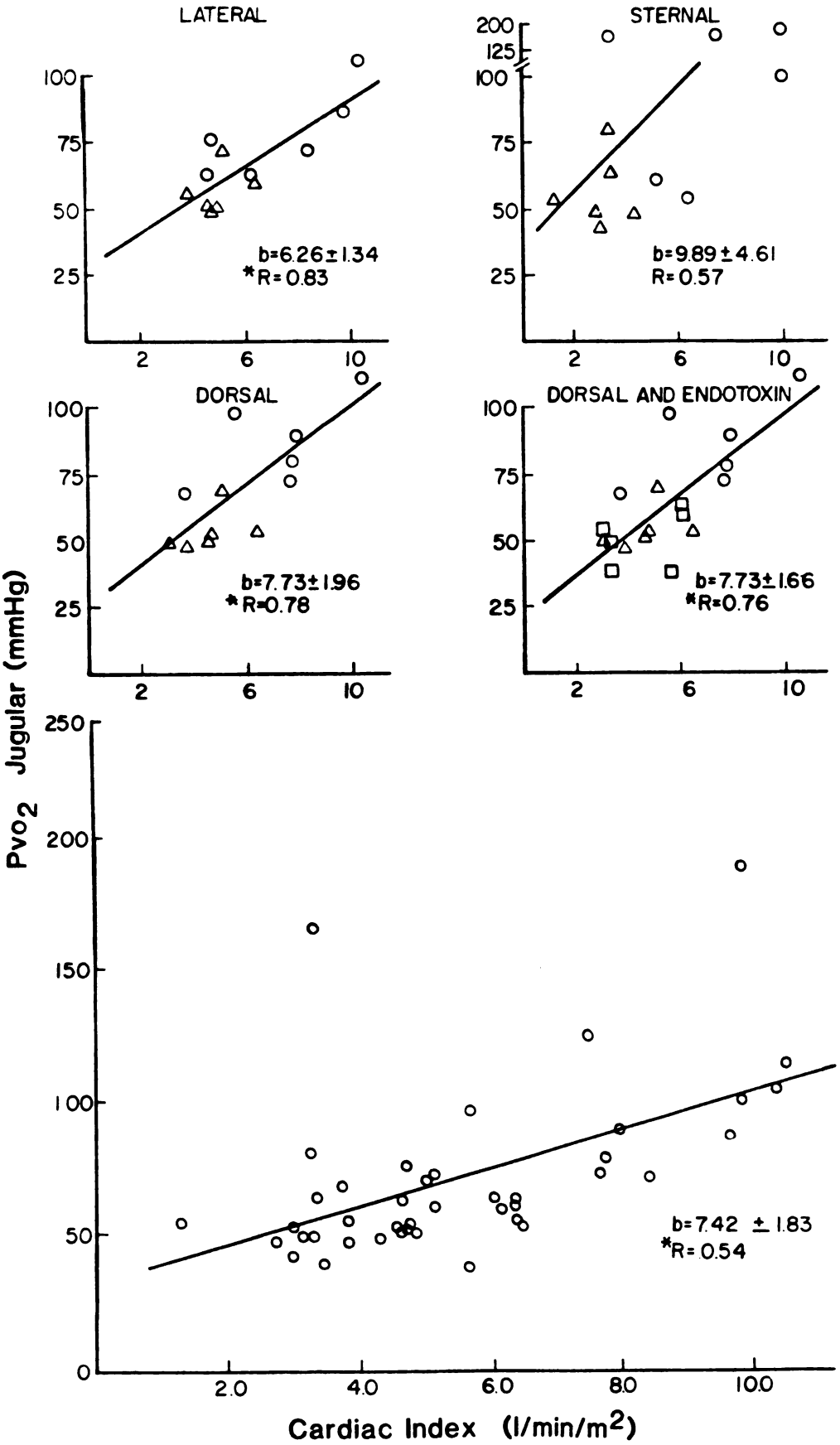

LATERAL
b=6.26±1.34
*R=0.83
STERNAL
b=9.89±4.61
R=0.57
DORSAL
b=7.73±1.96
*R=0.78
DORSAL AND ENDOTOXIN
b=7.73±1.66
*R=0.76
Pvo2 Jugular (mmHg)
b=7.42 ±1.83
*R=0.54
Cardiac Index (l/min/m2)

Figure 4.

The relationship between peripheral venous O_2 tension (PV_{O2} PERIPH) and cardiac index (CI). Measurements in six horses in lateral, sternal, and dorsal recumbencies and in dorsal recumbency after endotoxin administration are shown on upper panels; cumulative data are shown in lower panel. Regression coefficient (b) ± SE of the regression coefficient. Significant b and R values are indicated (*). (Δ = xylazine, O = dobutamine, □ = endotoxin.)

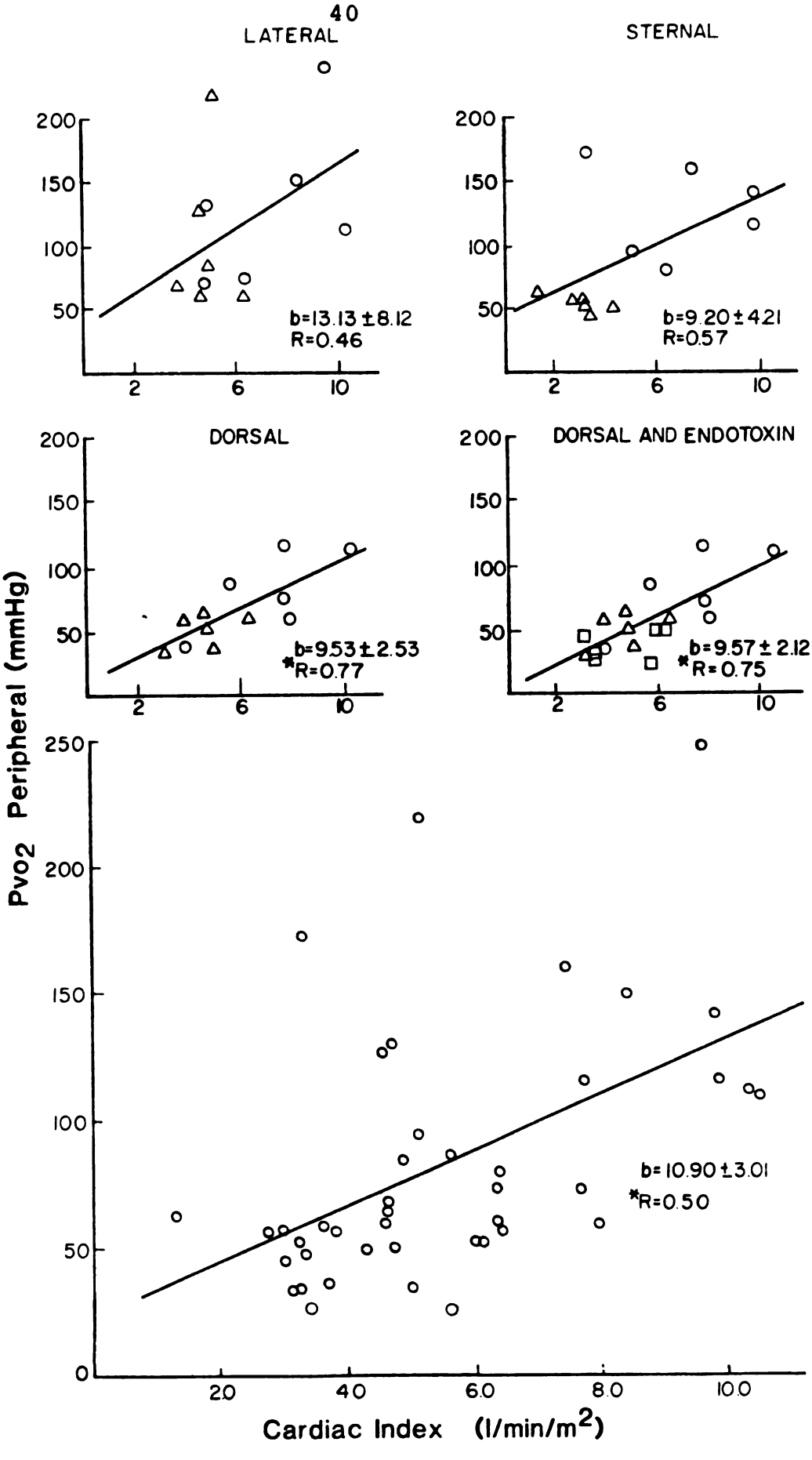

LATERAL
b=13.13 ±8.12
R=0.46
STERNAL
b=9.20 ±4.21
R=0.57
DORSAL
b=9.53 ±2.53
*R=0.77
DORSAL AND ENDOTOXIN
b=9.57 ± 2.12
*R=0.75
b=10.90 ±3.01
*R=0.50
Pvo2 Peripheral (mmHg)
Cardiac Index (l/min/m2)

Figure 5.

The relationship between heart rate (HR) and cardiac index (CI). Measurements in six horses in lateral, sternal, and dorsal recumbencies and in dorsal recumbency after endotoxin administration are shown on upper panels; cumulative data are shown in lower panel. Regression coefficient (b) ± SE of the regression coefficient. Significant b and R values are indicated (*).
(Δ = xylazine, O = dobutamine, □ = endotoxin, bpm = beats per minute.)

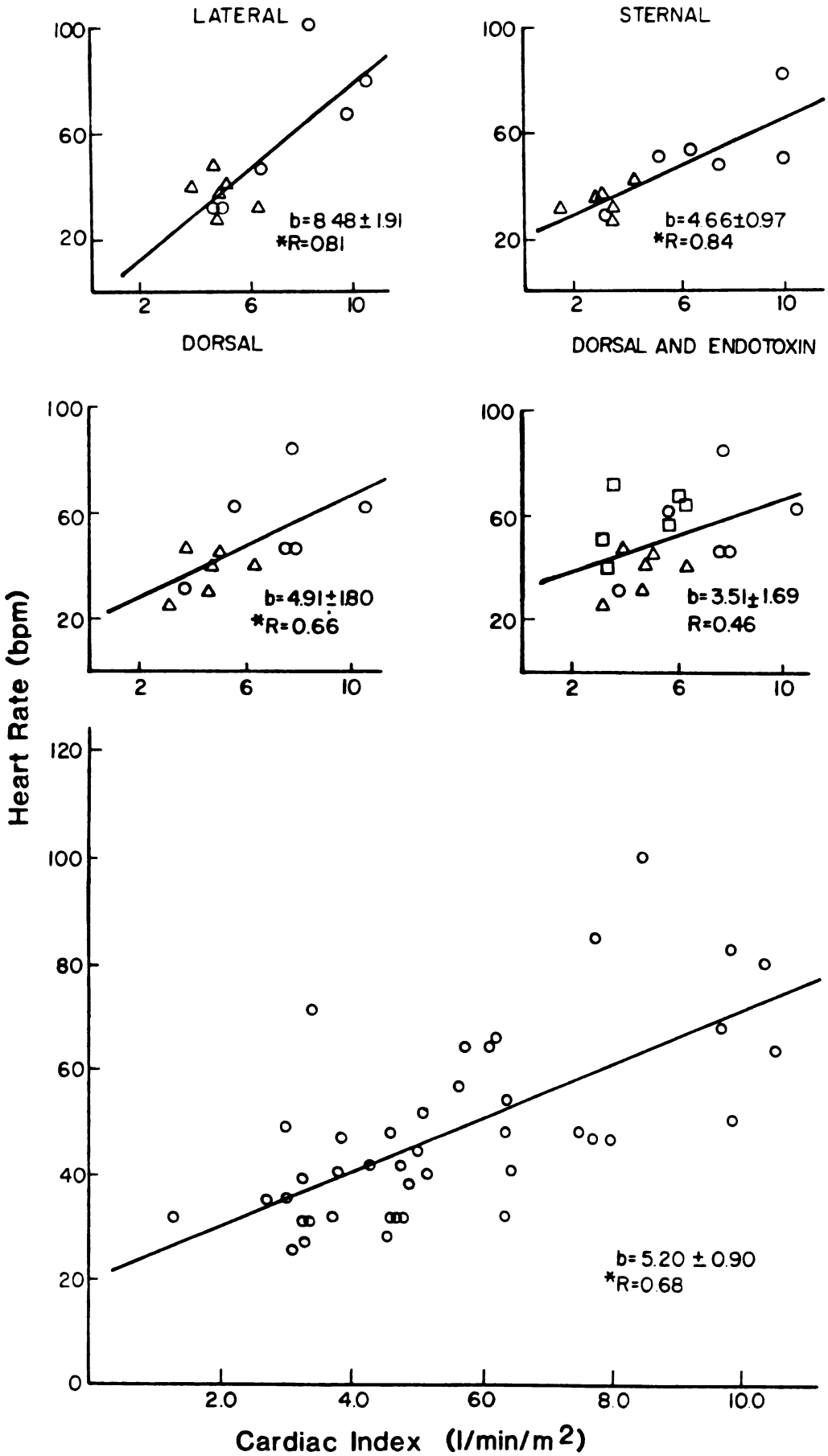

LATERAL
b=8.48±1.91
*R=0.81
STERNAL
b=4.66±0.97
*R=0.84
DORSAL
b=4.91±1.80
*R=0.66
DORSAL AND ENDOTOXIN
b=3.51±1.69
R=0.46
Heart Rate (bpm)
b=5.20 ± 0.90
*R=0.68
Cardiac Index (l/min/m2)

Figure 6.

The relationship between mean arterial blood pressure (MAP) and cardiac index (CI). Measurements in six horses in lateral, sternal, and dorsal recumbencies and in dorsal recumbency after endotoxin administration are shown on upper panels; cumulative data are shown in lower panel. Regression coefficient (b) ± SE of the regression coefficient. All b and R values are significant. (Δ = xylazine, O = dobutamine, □ = endotoxin.)

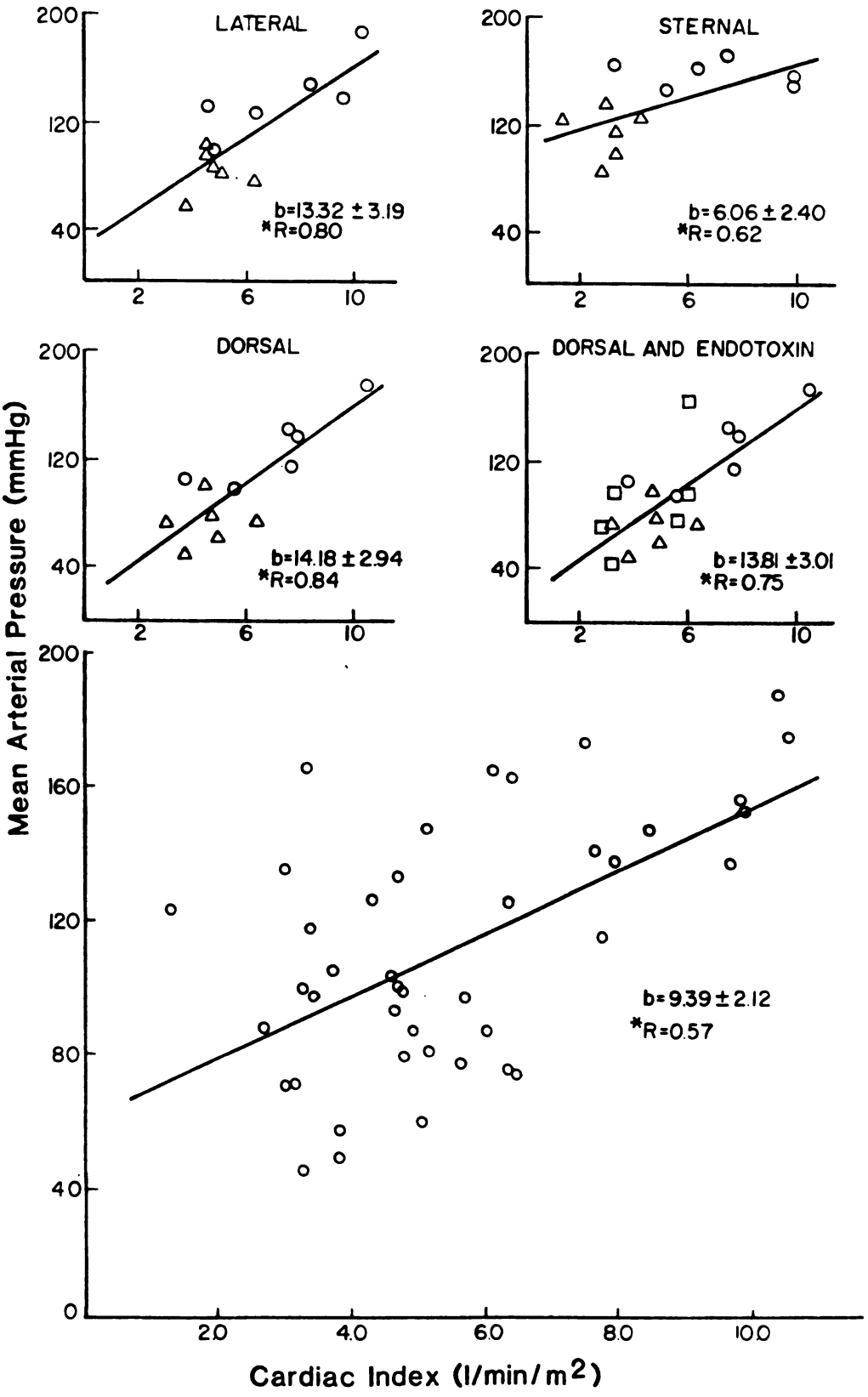

LATERAL
b=13.32 ± 3.19
*R=0.80
STERNAL
b=6.06 ± 2.40
*R=0.62
DORSAL
b=14.18 ± 2.94
*R=0.84
DORSAL AND ENDOTOXIN
b=13.81 ± 3.01
*R=0.75
b=9.39 ± 2.12
*R=0.57
Mean Arterial Pressure (mmHg)
Cardiac Index (l/min/m2)

Table 4.

The R values for linear regression analysis of CO or CI and cardiovascular variables.

Variable	CO (ml/kg/min)	CI (L/min/m^2)
$P\bar{v}_{O_2}$	0.66	0.66
HR	0.69	0.68
MAP	0.57	0.57
$P_{v_{O_2}}$ JUG	0.53	0.54
$P_{v_{O_2}}$ PERIPH	0.49	0.50

CO = cardiac output, CI = cardiac index, $P\bar{v}_{O_2}$ = mixed venous O_2 tension, HR = heart rate, MAP = mean arterial blood pressure, $P_{v_{O_2}}$ JUG = O_2 tension of blood from the jugular vein and $P_{v_{O_2}}$ PERIPH = O_2 tension of blood from a superficial limb vein.

All R values statistically significant.

Table 5.

The R values for linear regression analysis of cardiac index and cardiovascular variables in each recumbency.

Variable	Lateral	Sternal	Dorsal	Dorsal and Endotoxin
$P\bar{V}_{O_2}$	0.85*	0.78*	0.89*	0.85*
$P_{V_{O_2}}$ JUG	0.83*	0.57	0.78*	0.76*
$P_{V_{O_2}}$ PERIPH	0.46	0.57	0.77*	0.75*
HR	0.81*	0.84*	0.66*	0.46
MAP	0.80*	0.62*	0.84*	0.75*

$P\bar{V}_{O_2}$ = mixed venous oxygen tension, $P_{V_{O_2}}$ JUG = jugular venous oxygen tension, $P_{V_{O_2}}$ PERIPH = Superficial limb vein oxygen tension, HR = heart rate, and MAP = mean arterial blood pressure in different recumbencies and in dorsal recumbency after endotoxin administration.

* Significant R values.

DISCUSSION

The present study demonstrates that $P\bar{v}_{O_2}$ was significantly correlated with CI in anesthetized horses. Moffitt et al describes a significant correlation between mixed venous oxygen saturation ($S\bar{v}_{O_2}$) and perfusion index ($L/min/m^2$) in human patients on a cardiopulmonary bypass machine. The correlation between $S\bar{v}_{O_2}$ or $P\bar{v}_{O_2}$ and CI have been confirmed in a variety of clinical settings. (Stanley and Isern-Amaral, Armstrong et al, Parr et al, Kohanna et al, Dyson et al, de la Rocha et al, Muir AL et al, and Kasnitz et al). When $S\bar{v}_{O_2}$ decreases to <60% or if $P\bar{v}_{O_2}$ is decreased to 30 mmHg, the occurrence of death because of acute cardiac failure increases significantly (Armstrong et al; Kasnitz et al). In most studies, these values of $S\bar{v}_{O_2}$ and $P\bar{v}_{O_2}$ correlate with a CI of 2 $L/min/m^2$ (Parr et al; Kasnitz et al). In the present study, a $P\bar{v}_{O_2}$ of 40 mmHg correlated with a mean CI of 2 $L/min/m^2$.

Xylazine and dobutamine were administered to give a wide range of CI values over which to test the correlation between CI and $P\bar{v}_{O_2}$. Xylazine was used to decrease CI whereas dobutamine increased CI. Administration of xylazine IV induces transient second degree AV blocks and depresses HR (Kerr et al). Systemic arterial blood pressure rises initially, then gradually decreases to less than base line

values (Kerr et al). Peripheral vascular resistance increases twenty minutes after IM injection of xylazine at 2 mg/kg (McCashin and Gabel). In the present study, CI decreased five to ten minutes after IV xylazine administration compared with the CI values calculated after dobutamine administration. Second degree AV blocks did not occur immediately after xylazine administration.

Dobutamine increases CI and may also increase systemic arterial blood pressure and the rate of development of left ventricular pressure (dp/dt); there is no change in total peripheral vascular resistance (Swanson et al). Effects on HR are variable depending on the horse and the dose administered (Swanson et al). Sinus bradycardia occurs frequently with infusion rates of 3 to 5 µg of dobutamine/kg/min and a second degree AV block has been reported in one horse (Swanson et al). In the present study, dobutamine consistently increased CI as compared with CI values calculated after xylazine administration. Second degree AV blocks occurred in four horses during dobutamine administration. Previous xylazine administration may have been partially responsible for the high occurrence of this arrhythmia (Kerr et al).

In critical equine colic patients, endotoxemia is frequently present. After administration of anesthetic agents, CO may be further depressed (McDonell). In the present study, endotoxin was administered and the

relationship between $P\bar{v}_{O_2}$ and CI was evaluated. Endotoxin administration (200 µg/kg) results in an increased HR and MAP and a decreased CO fifteen minutes after administration (Bottoms et al; Burrows). In the present study, endotoxin increases HR, but did not change CO or MAP. This difference is likely related to the lower dose of endotoxin.

There is a significant correlation between HR and CO in resting and exercising horses (r = 0.91) (Bergsten). In the present study, the correlation between HR and CI was significant (r = 0.68) and HR of twenty-five beats per minute correlated with a CI of 2 L/min/m^2; however, endotoxin administration significantly increased HR without changing CI, resulting in an insignificant correlation between HR and CI. This finding may have clinical importance because many horses with severe gastrointestinal disease, which are anesthetized, have endotoxemia (Moore).

The $P\bar{v}_{O_2}$ was significantly correlated with CI in our anesthetized horses regardless of positioning. In addition, the correlation between $P\bar{v}_{O_2}$ and CI was unaltered by endotoxin administration. Whereas, HR and $P\bar{v}_{O_2}$ are significantly correlated with CI in the healthy anesthetized horse, only $P\bar{v}_{O_2}$ correlates with CI in anesthetized horses after endotoxin administration.

THE MAP was also significantly correlated with CI but the data points were poorly grouped, making it

difficult to derive a specific CI value for a measured MAP. Therefore, MAP was not as good an estimate of CI in anesthetized horses as was $P\bar{v}_{O_2}$.

Because a catheter must be placed in the pulmonary artery to collect mixed venous blood, we also evaluated the correlation between Pv_{O_2} in the jugular blood or blood obtained from superficial limb veins and CI. In horses in lateral and sternal recumbency, Pv_{O_2} PERIPH did not correlate with CI, whereas in horses in sternal recumbency, Pv_{O_2} JUG and CI did not correlate. Therefore, Pv_{O_2} PERIPH and Pv_{O_2} JUG were poor indicators of CO in anesthetized horses.

Cardiovascular changes resulting from sternal recumbency were noticed. The decreased SV and CO may be attributed to mechanical interference with venous return or CO. Sympathetic response to the decreased CO would account for the increased PVR, although an increased HR would also be expected. This was not observed.

The $\dot{V}O_2$ in our anesthetized horses ranged from 1.78 ± 0.13 to 1.89 ± 0.17 ml/kg/min and was unaffected by positioning. These values are slightly lower than those predicted for conscious horses (Brody). This slight difference may be explained by the effects of general anesthesia (Mikat et al).

Present CO values ranged from 39.1 ± 5.1 to 64.0 ± 4.3 ml/kg/min. These values are comparable with results of

studies (Hillidge and Lees) in which CO in halothane-anesthetized ponies ranged from 51.7 ± 8.7 to 68.9 ± 6.1 ml/kg/min and CO in anesthetized horses was 46.3 ml/kg/min (Gillespie et al).

In anesthetized horses, CO is frequently depressed because of the myocardial depressant effects of anesthetic agents or because of decreased venous return caused by positive pressure ventilation (Lumb and Jones). A low CO contributes to the severity of alveolar-arterial O_2 tension gradients in horses with intrapulmonary shunts (Gillespie et al; Kelman et al) and may have a role in the pathogenesis of postanesthetic recumbency myopathy (Lindsay et al). To prevent these complications, monitoring of CO and parameters that reflect CO is useful because it allows for early detection and treatment of low output states. In clinical practice, measurement of CO is difficult; therefore, measurement of $P\bar{v}_{O_2}$, which reflects CO, may be a useful adjunct to the management of anesthetized horses.

CONCLUSIONS

From results presented in this thesis the following conclusions can be made:

1) A significant statistical correlation can be made between $S\bar{v}_{O_2}$ ($P\bar{v}_{O_2}$ or A-VO_2) and CO because of the relationship described in the Fick Principle. This relationship does not allow accurate calculation of CO without measurement of all variables included in this principle. An estimation of CO from $S\bar{v}_{O_2}$, $P\bar{v}_{O_2}$ and A-VO_2 can be made in patients that are known to have stable metabolic and respiratory function.
2) Continuous monitoring is more useful than intermittent monitoring of $S\bar{v}_{O_2}$ and $P\bar{v}_{O_2}$ because it allows these measurements to be used as early indicators of changes in cardiorespiratory function. A decrease in $P\bar{v}_{O_2}$ or $S\bar{v}_{O_2}$ indicates the need for further diagnostics.
3) There is a statistically significant relationship between $P\bar{v}_{O_2}$ and CI in anesthetized horses regardless of position of the horse or the presence of endotoxin.

4) In anesthetized horses $\dot{V}O_2$ does not vary enough to interfere with the significant correlation between $P\bar{v}_{O_2}$ and CI.

5) Oxygen tension of blood from the jugular vein or from a superficial limb vein does not consistently correlate with CI so is not useful in estimation of CI.

6) Heart rate does not reflect the CO in anesthetized horses given a bolus of endotoxin.

7) Mean arterial blood pressure cannot accurately be used in estimation of CI because of the wide scatter of data points around a particular CI value.

FOOTNOTES

[a]Edwards Laboratories, Santa Ana, Calif.

[b]PE240, Intramedic, Clay Adams, Parsippany, NJ.

[c]P23 series, Gould Inc. Oxnard, Calif.

[d]Series 702, Spacelabs Inc. Chatsworth, Calif.

[e]Cordis Corp, Miami, Fla.

[f]Aire-Cuf, Bivona Inc, Gary, Ind.

[g]Warren E. Collins Inc, Braintree, Mass.

[h]Sodasorb, W.R. Grace and Co, Lexington, Mass.

[i]Hudson, Temecula, Calif.

[j]ABL1, Radiometer, Copenhagen NV, Denmark.

[k]Cathlon IV, Critkon, Tampa, Fla.

[l]Rompun, Haver Lockhart, Shawnee Mission, Kan.

[m]Vetalar, Parke-Davis, Morris Plains, NJ.

[n]Aceto Chemical Co, Inc, Flushing, NY.

[o]Bio-tal, Bio-Cutic, St. Joseph, Mo.

[p]Dobutrex, Eli Lilly, Indianapolis, Ind.

[q]5000b, Valley Labs, Boulder, Co.

[r]Sigma Chemical Co, St. Louis, Mo.

LIST OF REFERENCES

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