Hemodynamic effects in dogs after intramuscular administration of a combination of dexmedetomidine-butorphanol-tiletamine-zolazepam or dexmedetomidine-butorphanol-ketamine

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Objective—To evaluate hemodynamic effects in dogs after IM administration of dexmedetomidine (7.5 µg/kg), butorphanol (0.15 mg/kg), and tiletamine-zolazepam (3 mg/kg [DBTZ]) or dexmedetomidine (15 µg/kg), butorphanol (0.3 mg/kg), and ketamine (3 mg/kg [DBK]).

Animals—5 healthy adult mixed-breed dogs.

Procedures—Each dog received DBTZ and DBK in a randomized crossover study with a 48-hour interval between treatments. Anesthesia was induced and maintained with sevoflurane in 100% oxygen while instrumentation with Swan-Ganz and arterial catheters was performed. Following instrumentation, hemodynamic measurements were recorded at 3.54% (1.5 times the minimum alveolar concentration) sevoflurane; then sevoflurane administration was discontinued, and dogs were allowed to recover. Six hours after cessation of sevoflurane administration, baseline hemodynamic measurements were recorded, each dog was given an IM injection of DBTZ or DBK, and hemodynamic measurements were obtained at predetermined intervals for 70 minutes.

Results—DBTZ and DBK induced hypoventilation (Pa\(_{2}\), approx 60 to 70 mm Hg), respiratory acidosis (pH, approx 7.2), hypertension (mean arterial blood pressure, approx 115 to 174 mm Hg), increases in systemic vascular resistance, and reflex bradycardia. Cardiac output, oxygen delivery, and oxygen consumption following DBTZ or DBK administration were similar to those following sevoflurane administration to achieve a surgical plane of anesthesia. Blood \(l-lactate\) concentrations remained within the reference range at all times for all protocols.

Conclusions and Clinical Relevance—In healthy dogs, both DBTZ and DBK maintained oxygen delivery and oxygen consumption to tissues and blood lactate concentrations within the reference range. However, ventilation should be carefully monitored and assisted when necessary to prevent hypoventilation. (Am J Vet Res 2012;73:1363–1370)

Injectable anesthetic combinations continue to be used in veterinary anesthesia and surgery and are frequently used for specific programs, such as trap-neuter-release programs, working dog programs, and high-volume spay-neuter programs. Approximately 13.3 million surgeries were performed on dogs and cats at small animal veterinary practices in the United States in 2009, of which 63.4% were elective ovariohysterectomies and castrations. Many of those surgeries were performed with the use of combinations of injectable anesthetics or combinations of injectable anesthetics and inhalation anesthesia. In dogs, 2 commonly used anesthetics or combinations of injectable anesthetics and inhalation anesthesia.

Abbreviations

- CO: Cardiac output
- DAP: Diastolic arterial blood pressure
- DBK: Dexmedetomidine-butorphanol-ketamine
- DBTZ: Dexmedetomidine-butorphanol-tiletamine-zolazepam
- \(D_0\): Oxygen delivery
- HR: Heart rate
- MAC: Minimum alveolar concentration
- MAP: Mean arterial blood pressure
- OER: Oxygen extraction ratio
- SAP: Systolic arterial blood pressure
- SV: Stroke volume
- SVR: Systemic vascular resistance
- \(V_O2\): Oxygen consumption

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combinations of injectable anesthetics are DBTZ and DBK. On the basis of cardiorespiratory responses in dogs following administration of DBTZ or DBK, both combination treatments were determined to be effective and safe.

In studies conducted to evaluate hemodynamic effects, CO and oxygen content are measured in mixed-venous and arterial blood samples. Those measurements can then be used to calculate \( D_O \) and \( V_O \) for tissues. When the oxygen demand of tissues is greater than the oxygen supply to tissues, anaerobic metabolism begins, which results in increased blood lactate concentrations. Comparison of hemodynamic variables and blood lactate concentrations achieved over time after administration of various anesthetic agents or anesthetic combinations provides an effective method for the evaluation of the safety of the anesthetic protocol used. Studies of the hemodynamic effects in dogs after administration of dexmedetomidine alone and tiletamine-zolazepam alone have been performed. A single dose of dexmedetomidine administered to isoflurane-anesthetized dogs reduced CO and substantially increased SVR. Administration of tiletamine-zolazepam (6.6, 13.2, or 19.8 mg/kg, IV) resulted in an increased HR at all doses and increased CO at the 2 higher doses. Results of another study indicated that dexmedetomidine decreased perioperative myocardial lactate concentrations in dogs. To our knowledge, studies to evaluate the hemodynamics and blood lactate concentration of dogs following administration of the injectable anesthetic combinations DBTZ and DBK have not been conducted. Therefore, the objective of the study reported here was to compare hemodynamic variables, \( D_O \), \( V_O \), and blood lactate concentration in dogs following IM administration of DBTZ and DBK.

**Materials and Methods**

**Animals**—Five healthy mixed-breed dogs (2 females and 3 males) were used in the study. All dogs were 2 years old, and mean \( \pm \) SEM weight was 19.3 \( \pm \) 1.7 kg. Each dog was considered healthy on the basis of history and results obtained via a physical examination, CBC, and biochemical analysis. Food but not water was withheld from each dog for 12 hours prior to anesthesia. The study was approved by the Purdue University Animal Care and Use Committee.

**Study design**—The study was designed as a randomized crossover study, in which 2 injectable anesthetic combinations, DBTZ and DBK, were administered IM with a 48-hour washout interval between treatments. The DBTZ treatment consisted of dexmedetomidine (7.5 \( \mu \)g/kg), butorphanol tartrate (0.15 mg/kg), and tiletamine-zolazepam (3.0 mg/kg). The DBK treatment consisted of dexmedetomidine (15 \( \mu \)g/kg), butorphanol (0.3 mg/kg), and ketamine hydrochloride (3.0 mg/kg). Dogs were anesthetized with sevoflurane for instrumentation. Following instrumentation, hemodynamic measurements were obtained 5 minutes after a surgical plane of anesthesia was achieved via administration of sevoflurane alone; immediately prior to administration of each treatment (DBTZ or DBK; time 0 [baseline]); and 5, 10, 20, 30, 45, 60, and 70 minutes after administration of each treatment.

**Anesthesia for instrumentation**—For each dog, anesthesia was induced with sevoflurane in 100% oxygen administered via a face mask until tracheal intubation could be achieved. Following intubation, each dog was allowed to breathe spontaneously, and anesthesia was maintained by the use of sevoflurane and a circle anesthesia system while instrumentation was performed. Each dog was positioned in right lateral recumbency on a warm water circulating blanket; additionally, a warm air blanket was used to maintain body temperature within the reference range (37.2°C to 38.8°C). Instrumentation included a 22-gauge catheter inserted percutaneously into a dorsal pedal artery for continuous monitoring of arterial blood pressure and for collection of arterial blood samples. A 5F Swan-Ganz catheter was aseptically inserted into the left jugular vein and advanced into the lumen of the pulmonary artery; its position was confirmed by a characteristic pressure waveform and pressure values detected via an electronic monitor. The electronic monitor included a pressure transducer, capnography, pulse oximeter, and ECG machine such that direct arterial blood pressure, end-tidal sevoflurane and carbon dioxide concentrations, blood hemoglobin saturation for oxygen, and HR and rhythm (via lead II) were monitored continuously throughout the remainder of the anesthesia session.

Once instrumentation was completed, a surgical plane of anesthesia was achieved for each dog by increasing the amount of sevoflurane that was being administered such that the end-tidal concentration of sevoflurane was 1.5 MAC (3.54%). Anesthesia was stabilized at that concentration of sevoflurane for 5 minutes, and then a single set of hemodynamic measurements was recorded. Each dog was then disconnected from the electronic monitor, the arterial and Swan-Ganz catheters were bandaged in place, and each dog was allowed to recover from anesthesia and rest for 6 hours. The instrumentation and data collection for each dog during sevoflurane-induced anesthesia were completed within 60 minutes.

**Hemodynamic measurements**—Heart rate was obtained via the ECG lead II component of the electronic monitor. Direct blood pressures (SAP, DAP, and MAP) were obtained via an arterial blood pressure transducer that was connected to the catheter in the dorsal pedal artery and attached to the electronic monitor; the transducer and monitor were calibrated and zeroed to the midpoint of the thorax prior to use on each dog. Cardiac output was determined via a thermodilution technique. Briefly, 3 mL of chilled 5% dextrose solution was administered into the right atrium via the Swan-Ganz catheter over a period of 2 seconds, after which CO was measured by use of a CO computer. At each data collection time, CO was measured 3 to 4 times and the mean of the 3 most similar values was calculated and recorded. Measurements of core body temperature, mean central venous pressure, mean pulmonary artery pressure, and mean pulmonary artery wedge pressure were obtained directly by means of the Swan-Ganz catheter that was connected to the electronic monitor.
All equipment was calibrated and zeroed prior to use for obtaining measurements from each dog. At each data collection time, an arterial blood sample (2 mL) was obtained via the catheter in the dorsal pedal artery and anaerobically collected into a polypropylene syringe that had been rinsed with heparin; these arterial samples were used for blood gas analysis (\(P_{\text{aO}_2}\), \(P_{\text{aCO}_2}\), arterial bicarbonate concentration, and pH) and the calculation of arterial oxygen content. A mixed-venous blood sample (2 mL) was anaerobically collected via the Swan-Ganz catheter into a polypropylene syringe that had
been rinsed with heparin; these mixed-venous samples were used for blood gas analysis (mixed-venous partial pressure of oxygen, mixed-venous partial pressure of carbon dioxide, and pH), measurement of PCV, calculation of venous oxygen content, and measurement of hemoglobin and lactate concentrations. Hemoglobin concentration was calculated as the PCV measured in a sample divided by 3 and reported as the volume percentage. The lactate concentration was measured by means of a commercially available meter that had been validated for use in dogs. Blood samples used for blood gas analyses were stored at room temperature (approx 22°C) and analyzed within 30 minutes after collection.

The following hemodynamic variables were calculated from measured values: SV, SVR, pulmonary vascular resistance, arterial oxygen content, venous oxygen content, Do2, Vo2, and OER (Appendix). Oxygen saturation values for both arterial and mixed-venous blood samples were calculated from results obtained via blood gas analyses.

Administration of DBTZ or DBK—Six hours after cessation of sevoflurane administration, each dog was positioned in right lateral recumbency and reconnected to the electronic monitor. The position of the Swan-Ganz catheter was validated in a similar manner as previously described, and baseline hemodynamic measurements were obtained. Each dog then received DBTZ or DBK in accordance with a randomized assignment. Immediately prior to injection of each combination, the drugs were aspirated into separate syringes and then were mixed in 1 syringe for IM administration in the right or left quadriceps femoris muscle. Following treatment administration, 100% oxygen was provided to each dog via a face mask until tracheal intubation could be achieved (generally 2 to 3 minutes after injection), after which oxygen was provided via the endotracheal tube for the remainder of the anesthesia session. After the last hemodynamic measurements were obtained (70 minutes after treatment administration) for the first treatment, the catheters were bandaged in place and each dog was allowed to recover from anesthesia. Following a 48-hour washout interval, the procedure was repeated for the other treatment. After the final hemodynamic measurements were obtained for the second treatment, the arterial and Swan-Ganz catheters were removed and each dog was allowed to recover from anesthesia.

Statistical analysis—All data were reported as mean ± SEM, and all statistical analyses were conducted by means of statistical software. A 2-way ANOVA for repeated measures was used to evaluate treatment effects. An autoregressive with period 1 covariance structure was used to model intra-subject correlations.
The treatment effect of DBTZ was compared with that of DBK at each time by means of an a priori contrast. Similarly, the treatment effects of DBTZ or DBK at 20 minutes after administration were compared with the treatment effects of 3.54% (1.5 MAC) sevoflurane. For all analyses, values of $P < 0.05$ were considered significant.

Results

Cardiovascular effects of DBTZ and DBK treatments—Heart rate decreased significantly from the baseline value for both treatments; however, no significant differences in HR, mean pulmonary arterial pressure, and mean pulmonary arterial wedge pressure were detected between the DBTZ and DBK treatments at any time (Figure 1; Table 1). For the DBTZ treatment, SAP was increased significantly from the baseline value at 5 and 10 minutes, whereas for the DBK treatment, SAP was increased significantly from the baseline value at 5, 10, and 20 minutes. For both treatments, DAP was increased significantly from the baseline value at 5 and 10 minutes; for the DBK treatment, SAP was increased significantly from the baseline value at 5, 10, and 20 minutes. For both treatments, DAP was increased significantly from the baseline value at 5, 10, 20, 30, and 45 minutes, and MAP was increased significantly from the baseline value at 5, 10, 20, and 30 minutes. The CO, $\Delta t$, and $V_{\text{O2}}$ for both treatments were decreased significantly from the baseline values throughout the 70-minute observation period (Table 2). For the DBTZ treatment, SV was decreased significantly from the baseline value at 5 and 10 minutes, whereas for the DBK treatment, SV was decreased significantly from the baseline value at 5, 10, and 20 minutes. The SVR for both treatments was significantly throughout the observation period. The mean pulmonary arterial pressure was significantly increased from the baseline value at various times for both treatments. For the DBTZ treatment, OER was significantly increased from the baseline value at 5 and 10 minutes, whereas for the DBK treatment, OER was significantly increased from the baseline value throughout the observation period and was significantly higher than the OER for the DBTZ treatment at 5, 20, 30, 45, 60, and 70 minutes. The core body temperature for all dogs remained within reference limits throughout the study.

Pulmonary effects of DBTZ and DBK treatments—Results for arterial and mixed-venous blood gas analyses were summarized (Table 3). Both treatments resulted in a decrease in respiratory rate that resulted in hypoventilation and an increase in $\text{Paco}_2$ throughout the observation period. For the DBK treatment, PVR was significantly increased from the baseline value at...
30 and 70 minutes (Table 1). All mixed-venous blood l-lactate concentrations were within the reference range (0.82 to 1.32 mmol/L) and did not vary significantly from the baseline value at any time.

Cardiorespiratory effects 5 minutes after achieving a surgical plane of anesthesia with sevoflurane, compared with those at 20 minutes after administration of DBTZ or DBK—The mean ± SEM cardiorespiratory variables for dogs at 20 minutes after administration of DBTZ or DBK and after achieving a surgical plane of anesthesia for 5 minutes with sevoflurane (3.54%; 1.5 MAC) were summarized (Table 4). For the sevoflurane treatment, HR was significantly higher and SAP, DAP, MAP, and mean pulmonary arterial pressure were significantly lower, compared with those respective values for the DBTZ and DBK treatments. Additionally, the sevoflurane treatment resulted in a significantly higher Pao2 and a significantly lower SVR, OER, and mean pulmonary arterial wedge pressure, compared with those values for the DBK treatment.

Discussion

Both DBTZ and DBK have been used successfully as injectable anesthetic protocols for dogs undergoing surgical procedures with short durations (≤ 35 to 40 minutes).1-4 In the present study, the hemodynamic effects in dogs following the administration of DBTZ or DBK were compared, and the results were similar to those of other studies in which investigators evaluated the hemodynamic effects in dogs after administration of an α2-adrenoceptor agonist.5,6 Despite the fact that the DBK treatment contained twice the dose of dexmedetomidine as did the DBTZ treatment, it did not result in a significantly greater reduction in CO. That result was not unexpected because investigators of a study6 conducted to evaluate the hemodynamic effects in dogs after IM administration of medetomidine (5, 10, and 20 µg/kg, IV) in that study,16 peak SVR (mean ± SEM, 14,710 ± 1,330 dynes/cm²) was achieved. In the present study, peak SVR (9,234 ± 1,317 dynes/cm² for DBTZ and 12,732 ± 1,401 dynes/cm² for DBK) was detected at 5 minutes after treatment administration and represented a 6.3- and 7.8-fold increase from the baseline SVR for DBTZ and DBK, respectively.

In the present study, hypertension (MAP, 115 to 174 mm Hg) was detected for the first 30 minutes after both treatments; thereafter, MAP returned to baseline values. When an α2-adrenoceptor agonist is administered alone, severe hypertension does not generally develop. The hypertension in the dogs of the present study may have been caused by vasoconstriction induced by dexmedetomidine and the increase in HR and positive inotropic effects attributable to the dissociative drugs, which is a hemodynamic response similar to that when an anticholinergic drug is used to increase HR after administration of an α2-adrenoceptor agonist.6

Cardiac output decreased significantly from the baseline value after administration of DBTZ or DBK in the study reported here. The mean ± SEM CO was 0.9 ± 0.1 L/min for dogs that were anesthetized with dexmedetomidine (20 µg/kg, IV) and maintained at 0.26% end-tidal isoflurane.8 In the present study, the lowest CO (mean ± SEM, 1.2 ± 0.2 L/min) was recorded at 5 minutes after DBK administration. The reduction of CO observed in the present study could have been caused by a substantial increase in SVR that resulted in an increase in afterload that impeded ventricular outflow, reflex bradycardia induced by peripheral vasoconstriction, or a decrease in plasma catecholamine concentrations induced by dexmedetomidine that resulted in reduced inotropic support of myocardial contractility.13

A primary goal of anesthesia is to maintain adequate tissue perfusion with well-oxygenated blood.17

Adequate tissue perfusion with oxygenated blood is provided by a balance between Do2 and Vo2.18 When Do2 to tissue is inadequate (because of a lack of tissue perfusion, arterial hypoxemia, or both), cells within the tissue will use a variety of methods to compensate for hypoxia in an attempt to sustain energy production via aerobic metabolism.5,6,15,18 One method used to...

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crease $D_O_2$ to tissues is to increase the OER. If $D_O_2$ to tissue cannot be increased by the compensatory increase in OER, cells within the affected tissue will transition from aerobic to anaerobic metabolism, of which one of the by-products is l-lactate. In a study that involved pentobarbital-anesthetized dogs, when the baseline $V_O_2$ was 5.6 mL/kg/min, the critical $D_O_2$ (minimum $D_O_2$ required to prevent anaerobic metabolism) was estimated to be 9 to 10 mL/kg/min. In another study that involved pentobarbital-anesthetized dogs, the critical $D_O_2$ was 10.2 mL/kg/min and the critical OER (minimum OER required to prevent anaerobic metabolism) was 62%. When $D_O_2$ is less than the critical value, $V_O_2$ becomes supply dependent and lactic acidosis develops. In the present study, the lowest $D_O_2$ (mean ± SEM, 12.1 ± 2.0 mL/kg/min) and highest OER (40 ± 2%) were detected at 5 minutes after DBK administration, at which time the $V_O_2$ (4.7 ± 1.0 mL/kg/min) was the highest. The highest OER recorded in the present study was much lower than the critical OER (62%) in dogs reported by investigators of that other study. Thus, for the present study, the hemodynamic data and the fact that blood l-lactate concentrations remained within reference limits indicated that the tissues of the study dogs received adequate oxygen throughout the observation period regardless of the treatment (DBTZ or DBK) administered.

For DBTZ and DBK, the reasons $D_O_2$ was lowest and $V_O_2$ were highest at 5 minutes after treatment administration are unknown. A possible explanation may be that although the greatest magnitude of decrease in $CO$ and $D_O_2$ was detected at 5 minutes after treatment administration, the tissues had not yet had time to process this change and were still consuming oxygen at a higher rate. Oxygen consumption was lowest at 20 minutes after administration for both treatments and corresponded to the time at which the peak surgical plane of anesthesia was achieved for DBTZ or DBK in previous clinical studies.

Administration of DBTZ or DBK induced profound respiratory acidosis. The lowest arterial pH (7.19 for DBTZ and 7.20 for DBK) and highest $Pa_CO_2$ (75 mm Hg for DBTZ and 69 mm Hg for DBK), along with a concurrent decrease in respiratory rate, were detected at 10 minutes after administration. A decreased respiratory rate and tidal volume can be induced by all of the drugs used in the combination treatments. Even though the respiratory rates for both treatments were significantly lower than those at baseline, the study dogs remained well oxygenated ($Pa_O_2$ range, 215 to 436 mm Hg) throughout the observation period because of insufflation with 100% oxygen. The results of the present study indicated that dogs anesthetized with DBTZ or DBK should be provided supplemental 100% oxygen.

The primary objective of the present study was to compare the hemodynamic effects in dogs after IM administration of DBTZ or DBK, but we were also interested in comparing the hemodynamic effects in dogs after achieving a surgical plane of anesthesia via administration of sevoflurane with those after administration of DBTZ and DBK, respectively. On the basis of results of other studies conducted by our laboratory group, the anesthetic and analgesic effects of DBTZ or DBK peak at 20 minutes after administration and are equivalent to a surgical plane of anesthesia. Therefore, the hemodynamic effects in dogs after reaching a surgical plane of anesthesia with sevoflurane were compared with those achieved 20 minutes after administration of DBTZ or DBK. Sevoflurane induced a significantly higher HR and lower arterial blood pressure (SAP, DAP, and MAP) and SV, compared with those results for DBTZ or DBK. Sevoflurane induced a significantly lower SVR, compared with that of DBK. However, sevoflurane induced comparable CO, $D_O_2$, and blood l-lactate concentrations as those induced by DBTZ or DBK (Table 4).

Interestingly, the cardiovascular effects (ie, higher HR and lower SAP, DAP, and MAP) induced by sevoflurane were the opposite of those induced by DBTZ or DBK. This was attributable to the different hemodynamic responses between sevoflurane and dexmedetomidine-containing combinations. When anesthetized with sevoflurane, the dogs had a CO comparable to that when they were anesthetized with DBTZ or DBK. However, the cardiovascular response by which CO was maintained when dogs were anesthetized with sevoflurane was the opposite of that when dogs were anesthetized with DBTZ or DBK. Cardiac output was maintained via a lower SV and a higher HR when the dogs were administered sevoflurane, whereas CO was maintained via a higher SV and a lower HR when the dogs were administered DBTZ or DBK. Also, administration of DBTZ or DBK induced systemic vasoconstriction as evidenced by higher SVR and arterial blood pressure, which is in contrast to the sevoflurane-induced vasodilation as evidenced by lower blood pressure and SVR.

The results of the present study and those of another study suggest that the hemodynamic response in dogs may be more optimal if a lower dose of DBTZ or DBK is used in combination with an inhalation anesthetic, such as sevoflurane, to yield a more balanced cardiovascular response than that achieved with the higher doses of DBTZ or DBK used in the present study. However, further studies are needed to confirm this observation.

The hemodynamic profiles in dogs after IM administration of DBTZ or DBK were similar, particularly with regard to CO, $D_O_2$, and $V_O_2$, and characterized by hypertension, an increase in SVR, reflex bradycardia, and a minimal effect on blood l-lactate concentration. Hypoventilation and respiratory acidosis developed after DBTZ or DBK administration, but tissue hypoxia was prevented and improvements in $D_O_2$ were achieved by providing dogs with supplemental 100% oxygen.

g. Gaymar TP Professional, Gaymar Industries Inc, Orchard Park, NY.
h. Gaymar hot air hugger, Gaymar Industries Inc, Orchard Park, NY.
i. Serrulio Teflon IV catheter, 22-gauge, 1-inch, Terumo Medical Corp, Somerset, NJ.
k. Datascope DPM7, MindRay, Malwah, NJ.

1. PX260 pressure monitoring kit with TruWave transducer, Edwards Lifesciences Corp, Irvine, Calif.

m. COM-I CO computer, Edwards Lifesciences Corp, Irvine, Calif.

n. ABL5 analyzer, Radiometer Medical ApS, Brønshøj, Denmark.

o. Lactate Pro Meter, Arkray, Quesnel, BC, Canada.


References


Appendix

Equations used to calculate various hemodynamic variables in 5 healthy dogs after IV administration of DBTZ (dexmedetomidine [75 µg/kg]), butorphanol [0.15 mg/kg], and tiletamine-zolazepam [3 mg/kg]) or DBK (dexmedetomidine [15 µg/kg], [3 mg/kg]), and ketamine [3 mg/kg]).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Equation</th>
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<tbody>
<tr>
<td>SV (mL/beat)</td>
<td>CO/HR</td>
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<tr>
<td>SVR (dynes/cm²)</td>
<td>80 × (MAP – CVP)/CO</td>
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<tr>
<td>PVR (dynes/cm²)</td>
<td>80 × (MPAP – PAWP)/CO</td>
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<tr>
<td>CaO₂ (mL/dL)</td>
<td>(1.34 × SaO₂ × CHb) ± (0.005 × PaO₂)</td>
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<tr>
<td>CvO₂ (mL/dL)</td>
<td>(1.34 × SvO₂ × CHb) ± (0.005 × PaO₂)</td>
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<tr>
<td>DO₂ (mL/min)</td>
<td>10 × CaO₂ × CO</td>
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<tr>
<td>VO₂ (mL/min)</td>
<td>CO × (CaO₂ – CvO₂)</td>
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<tr>
<td>OER (%)</td>
<td>(CaO₂ – CvO₂) × 100/ CaO₂</td>
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CaO₂ = Arterial oxygen content, CHb = Hemoglobin concentration, CvO₂ = Venous oxygen content, CVP = Central venous pressure, MPAP = Mean pulmonary arterial pressure, PAWP = Mean pulmonary arterial wedge pressure, PaO₂ = Venous partial pressure of oxygen, PVR = Pulmonary vascular resistance, SaO₂ = Arterial oxygen saturation, SvO₂ = Venous oxygen saturation.