Measurement of cardiac output by transesophageal Doppler ultrasonography in anesthetized dogs - comparison with thermodilution

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Measurement of cardiac output by transesophageal Doppler ultrasonography in anesthetized dogs – comparison with thermodilution

by

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TABLE OF CONTENTS

CHAPTER 1. General Introduction 1
Thesis Organization 1
Introduction 1
Background and Significance 3
References 17

CHAPTER 2. Measurement of cardiac output by transesophageal Doppler ultrasonography in anesthetized dogs – comparison with thermodilution 23
Abstract 23
Introduction 25
Materials and Methods 26
Results 31
Discussion and Conclusion 32
Acknowledgement 35
References 36
Figures 39

CHAPTER 3. General Conclusions 46
General Discussion 46
Recommendations for Future Research 47

ACKNOWLEDGMENTS 49
CHAPTER 1. GENERAL INTRODUCTION

Thesis organization

This thesis is written in an alternative thesis format and contains three chapters: general introduction (Chapter 1), research paper (Chapters 2) and general discussion (Chapter 3). The general introduction includes a literature review concerning different techniques for cardiac output measurement. Chapter 2 is the article “Measurement of cardiac output by transesophageal Doppler ultrasonography in anesthetized dogs – comparison with thermodilution” which is to be submitted to the Journal Veterinary Anesthesia and Analgesia.

Introduction

The primary role of the cardiovascular system is to maintain normal blood flow and oxygen delivery to the tissues. Together with the respiratory system, the cardiovascular system is the major determinant of oxygen tissue delivery. It is known that high-risk human surgical patients (e.g. septicemia, massive acute blood loss, acute renal failure or respiratory failure) are likely to develop inadequate tissue oxygen concentrations for two reasons: decreased oxygen delivery and/or increased oxygen consumption. A lack of tissue oxygen leads to tissue hypoxia which can trigger the cellular production of cytokines (e.g. tumor necrosis factor, interleukins, histamine and serotonin) that are thought to initiate or intensify organ failure. The resulting cellular hypoxia causes the metabolism to switch from aerobic to anaerobic with the production of lactic acidosis. Cell hypoxia and reperfusion injury can lead to
cell death and finally death of the patient. Therefore, it is essential to monitor and support the cardiovascular system of critically ill patients undergoing general anesthesia and surgery.

The hemodynamic measurements frequently monitored in small animal veterinary clinics are: heart rate (HR), mean arterial blood pressure (ABP), electrocardiogram (ECG), arterial hemoglobin saturation with oxygen (SpO2) and central venous pressure (CVP). All of these parameters are useful but none of them directly evaluate tissue oxygenation. Although blood pH and lactate levels provide objective measurements to of inadequate tissue oxygenation they do not immediately reflect tissue hypoperfusion and tissue hypoxia. Identifying early undesirable hemodynamic changes are of tremendous importance for successful therapy. If adequate therapy is delayed until organ failure occurs the consequences are usually catastrophic. Therefore, in human critical care medicine and anesthesiology cardiac output (CO) measurement is an integral part of the preoperative, operative and postoperative care.

Cardiac output is the product of stroke volume and HR and is an indicator of the heart’s ability to pump blood to the peripheral tissues. A dynamic feature of the heart’s function, the CO depends on the interrelationship of myocardial contractility, preload, afterload and HR. In critically ill patients it is likely that some of these factors are altered resulting in poor myocardial performance. Since the cardiovascular system is a closed system none of these four factors are totally independent and in combination they determine the CO.
Thermodilution (TD) is a clinically accepted technique for monitoring CO in human medicine. The balloon tipped TD catheter, properly placed in the pulmonary artery, not only allows measurement of CO, but also gives information about pulmonary artery occlusion pressure (PAWP) and CVP. However, benefit/risk ratio of the technique has been questioned. In veterinary medicine TD is not widely utilized in clinical monitoring due to invasive nature of the catheterization, requirement of a trained and experienced clinician and the cost. Therefore in veterinary medicine, TD is mainly used for research purposes while the clinical hemodynamic monitoring is primarily based on the HR, ABP, ECG, SpO2, and CVP.

Transesophageal Doppler ultrasonography (TED) is one of the innovative techniques for CO monitoring. Although the equipment is expensive, it has potential use in veterinary medicine because it is non-invasive, gives real time and continuous data about cardiovascular function, and requires less expertise than TD.

The purpose of this project was to examine the accuracy of the TED technique in dogs by comparing TED and TD CO measurements. The CO of experimental dogs was altered by applying different pharmacological and mechanical treatments. If the TED technique is accurate it offers significant advantages over TD and could be a very useful tool for anesthesia monitoring in high-risk veterinary patients.

Background and significance

The practice of anesthesiology involves providing support for critically ill patients undergoing surgery. This includes intensive and accurate monitoring of
parameters that might answer the most important question: are the tissues sufficiently oxygenated or not? Unfortunately, critically ill patients in almost all situations have significantly compromised pulmonary and cardiovascular function which anesthetic drugs may compromise even further. Therefore, monitoring these patients is crucial and one of the biggest challenges in veterinary anesthesia practice. An accurate and easy to use method to measure cardiac output would be extremely beneficial.

In the early 70s, Shoemaker and colleagues described high-risk surgical human patients (e.g. septicemia, massive acute blood loss, acute renal failure, respiratory failure) that had postsurgical mortality rates between 30% and 40%\(^1\). Research identified therapeutic goals that improved the survival of these patients. One treatment was to increase CO and therefore oxygen delivery (DO\(_2\)) by the intravenous infusion of dopexamine hydrochloride which significantly reduced mortality and morbidity in the critically ill patients\(^2\). Increasing the DO\(_2\) to at least 600 ml/min per m\(^2\) resulted in a better prognosis and improved chances of survival. Williams and colleagues demonstrated that the oxygen (O\(_2\)) deficit was highest in the non-surviving patients, moderate in survivors with transient organ failure, and lowest in patients who survived with no organ failure\(^3\). Unfortunately, some pathological conditions alter not only the DO\(_2\) to the peripheral tissues but also the O\(_2\) utilization by the tissues. In septic shock patients severe tissue O\(_2\) deficits are due to impaired cardiovascular performance and increased metabolic rate\(^4\). In this condition O\(_2\) demands are much higher than under normal physiological conditions.
The beneficial effect of improved CO and therefore DO₂ in septic patients was evident by the reduction in mortality from 74% to 40%.

The DO₂ is the product of CO and arterial blood oxygen content (CaO₂), which depends on respiratory and cardiovascular system coordination. The lungs must effectively take the O₂ from the environment and move it into the blood while the cardiovascular system must provide sufficient flow of the oxygenated blood. The DO₂ is determined by many parameters of which only seven can be altered in an attempt to improve DO₂: hemoglobin concentration (Hb), SaO₂, HR, preload, myocardial contractility, mean arterial pressure (MAP) and total systemic vascular resistance (TSVR)⁵.

Red blood cells contain hemoglobin which binds and carries O₂ to the peripheral tissues. Since there is a very small amount of O₂ dissolved in the blood, CaO₂ mainly depends on the blood's Hb concentration because one gram of Hb binds 1.34 ml of O₂. Furthermore, the Hb concentration can be easily determined and transfusion with a Hb containing solution will rapidly increase its concentration.

The SaO₂ is the percent of the Hb in the blood that is saturated with O₂. The SaO₂ can be measured by co-oximeters and estimated by the pulse oximetry or blood gas analyzer. It can be improved by increasing a patient's inspired oxygen concentration (FiO₂), increasing alveolar ventilation, or reducing venous admixture.

The HR together with stroke volume (SV) determines CO. Heart rate is easy to assess and can be pharmacologically manipulated if significant bradycardia or tachycardia occurs.
Cardiac preload is one of the three determinants of stroke volume\(^6\). Preload determines the amount of stretch placed on the myocardial sarcomeres and is related to the quantity of blood that enters the ventricles during diastole (venous return to the heart) and ventricular compliance. Starling's law of the heart states that increased sarcomere stretch (increased blood volume in the ventricles) results in a more forceful contraction of the heart muscle to expel the increased volume. A decreased stretch results in the opposite effect\(^6\). Since there is no clinically relevant method for determining sarcomere fiber length, clinicians rely on physical examination findings or pressure measurements to estimate preload such as central venous pressure and PAWP. Unfortunately, physical examination and pressure measurements can be unreliable indicators of intravascular volume\(^6\).

Contractility is the ability of the heart to perform work (pump blood) and is entirely independent of preload and afterload. Parameters that are used as indicators of contractility are: ejection fraction (EF), peak velocity (PV) of blood flow in the aorta, acceleration (Acc) of the blood flow in the aorta, and dP/dt. Some of these indicators (e.g. EF, PV and Acc)\(^7\) can be estimated by echocardiography while others require cardiac catheterization (dP/dt).

Afterload is the force opposing ejection of blood from the ventricles during systole. The MAP and TSVR are the two clinical measurements available to evaluate afterload. The MAP is the most common afterload parameter monitored in veterinary clinical practice. Although it reflects the peripheral force opposing ejection of the blood from the heart and the driving force for tissue perfusion, it is not a measure of tissue blood flow. In clinical situations of low CO, MAP could be close to
normal physiological values due to reflex sympathetic vasoconstriction. When the MAP is low, the clinician usually assumes that tissue blood flow and perfusion are compromised and tries to correct the hypotension (fluid therapy, vasopressor or inotrope therapy).

Total systemic vascular resistance is also a component of the afterload. The TSVR can be calculated but it is not routinely applied in practice because the CO has to be measured. Although, TSVR can be very useful, there are situations in which TSVR is not equal to the afterload at all (e.g. patients with subaortic stenosis may have markedly increased afterload with normal or reduced TSVR).

The CO is the amount of blood pumped from one ventricle per unit of time and represents the blood circulating throughout the body. Preload, afterload, and myocardial contractility are highly integrated in determining the CO of the heart. Separate monitoring of each of these three parameters would be very useful but still, none of them provide an accurate indication of adequate perfusion or DO₂.

The CO measurement can be obtained by non-invasive and invasive methods. In the following pages we will describe basic characteristics of the most commonly used methods for the CO measurement.

1. Invasive methods
   a) Thermodilution

   Swan and Ganz first introduced the pulmonary artery catheter (PAC) in the early 1970’s⁸ for the measurement of CO by thermodilution. Today, PAC or Swan-Ganz PAC is described as the clinically acceptable method for measuring CO in
The Swan-Ganz catheter has an inflatable balloon, which enables it to be floated into the pulmonary artery through the right side of the heart, using the natural flow of the blood. Shortly after the original catheter was introduced into clinical practice, a thermistor was added, which allowed CO to be measured by thermodilution (TD). A thermal indicator (e.g. cold saline or 5% dextrose) of a known temperature is injected in the right atrium (proximal port of the catheter) and the resultant change in the temperature of the pulmonary artery blood is continuously recorded by a thermal sensor (termistor) mounted at the tip of the catheter. The computer uses different parameters obtained during recording to calculate the CO according to the following formula:

\[
\text{CO}_{TD} = \frac{\text{Vi} \times \text{ri} \times \text{Ci} \times (\text{Tb-Ti}) \times 0.825 \times 60}{\text{rb} \times \text{Cb} \times \int \text{DTb}(t) \, dt}
\]

CO – cardiac output (l/min); Vi – injectate volume (ml); Ti – injectate temperature (C); DTb – the temperature of blood injectate mixture at the distal termistor; rx and Cx are the specific gravity and heat of the blood (B) and injectate (I) respectively; 60 = 60 s/min; 0.825 = empirical correction factor for catheter warming. The expression \((\text{ri} \times \text{Ci} / \text{rb} \times \text{Cb})\) is a constant that is related to the type of injectate. For 5% dextrose it is equal to 1.08 and for saline it is equal to 1.0. The expression \((\text{DTb}(t)dt)\) equals the area under the temperature vs time curve and is the mean indicator of temperature change over time.

It has been shown that thermodilution correlates well with two other methods of CO measuring: Fick’s method and indicator dye dilution method. Besides the
CO, PAC provides other valuable measurements such as CVP and PAWP\textsuperscript{12}. When a pressure transducer is connected to the proximal port of the catheter located in the right atrium the CVP can be measured. By inflating the balloon in the pulmonary artery a wedge pressure can be obtained which estimates the left atrial pressure. Both of these parameters may provide insight into the vascular volume status of the patient and help in making decisions about fluid therapy. However, there are controversial reports about safety and accuracy of the Swan-Ganz catheter. Some groups reported a low incidence of morbidity and/or mortality associated with the PAC and a low risk-benefit ratio\textsuperscript{12,13}. On the contrary, there are many authors who are concerned about the complications associated with the catheter and have published risk-benefit analysis that revealed an increased morbidity and mortality in the patients\textsuperscript{14,15,16,17}. When the facts of an unclear risk-benefit ratio, the invasiveness of PAC placement, and the intermittent CO measurements are taken into consideration, it is not surprising that several new technologies are being proposed.

\textit{b) Fick oxygen method}

The Fick’s principle, applied to the CO measurement, states that the amount of \( \text{O}_2 \) uptake by an organ (\( \text{O}_2 \) consumption) depends on the blood flow (CO) to that organ and arteriovenous \( \text{O}_2 \) concentration difference\textsuperscript{10}. To measure the global CO, the \( \text{O}_2 \) consumption is measured as the difference of the \( \text{O}_2 \) concentration in the inspired and expired air\textsuperscript{18}. The arterial \( \text{O}_2 \) concentration is measured from the peripheral artery blood sample and venous \( \text{O}_2 \) concentration is measured from the
mixed venous blood sample obtained from the PA catheter\textsuperscript{19}. By calculating the ratio between oxygen consumption and the arteriovenous oxygen difference, the CO can be determined as shown in the formula\textsuperscript{10}:

\[
\text{Cardiac output (l/min)} = \frac{\text{Oxygen consumption (ml O}_2/\text{min)}}{\text{Arteriovenous oxygen difference (ml O}_2/\text{l blood)}}
\]

It has been shown that Fick’s method correlates well with thermodilution in dogs \(r^2=0.97\)\textsuperscript{20} but due to the technical demands and invasive nature of the procedure it is not widely accepted in veterinary medicine\textsuperscript{10}.

c) \textit{Indicator dilution method}

This CO measurement technique is based on the injection of an indicator of a known concentration in the right atrium or right ventricle and subsequent measurement of the concentration of the same indicator in the peripheral circulation (usually femoral artery) by an optical detector (densitometer)\textsuperscript{18}. The dilution of the indicator in the peripheral circulation depends on the blood flow (CO). It has been shown that the dye dilution method correlates well with thermodilution and the Fick method for CO measurement\textsuperscript{20} but it has been used mostly for research purposes because it is technically difficult, time consuming, and requires frequent blood sampling.
d) Lithium dilution method

Lithium dilution method is another type of dilution method which has been validated in the past 10 years\textsuperscript{21}. This method is based on the use of lithium as an alternative indicator for the CO measurement. Briefly, isotonic lithium-chloride, in a small dose (0.002-0.004 mM/kg) that does not have any pharmacological effect, is injected as a bolus in the right atrium or right ventricle. A change of the ion concentration is monitored by an ion-sensitive electrode attached to the arterial line manometer system in the periphery\textsuperscript{21}. Since lithium chloride concentration highly depends upon sodium and Hb concentration, these two parameters have to be independently measured and delivered to the computer for the precise estimation of the CO\textsuperscript{21}. It has been reported that the lithium dilution method can be a suitable method for CO measurement in dogs\textsuperscript{22}.

Invasive methods for the monitoring of CO are reliable. But necessitate cardiac catheterization carries a risk of eventual development of cardiac arrhythmia, damage to the endothelium of blood vessels, and subsequent thrombosis. Due to these reasons, it was important to develop devices and techniques, which would be reliable and non-invasive to determine the CO.

2. Non-invasive methods

Ultrasound monitoring methods have become an important area of research because they are non-invasive and safe. Ultrasound monitoring techniques are based on the Doppler effect\textsuperscript{23}. The Doppler effect is a change in ultrasound wave
frequency as the ultrasound wave is being reflected from a moving target. If the motion is toward the transducer, the frequency of the returning echo is higher than that of the transmitted ultrasound beam. If the motion is away from the transducer, the echoes have a lower frequency than the transmitted ultrasound beam. The difference between the transmitted and received frequencies is a Doppler shift. This is the basic principle behind all Doppler techniques for the measurement of CO regardless of the type of machine or position of the probe. The most frequently employed non-invasive monitoring techniques, which use the Doppler principle, are the transesophageal and transthoracic approaches.

a) Transesophageal approach

Transesophageal Doppler measurement of CO can be made from the left ventricular outflow tract, aortic valve, mitral valve, main pulmonary artery or the right ventricular outflow tract and descending aorta. Although, these techniques are not invasive, the accuracy has been questioned. The most frequently used approach is the measurement of the CO from the descending aorta.

In 1975 Diagle et al. proposed a new method for CO monitoring where ultrasound transducer was incorporated in the esophageal probe. Initially, the esophageal probe only had a Doppler ultrasound transducer incorporated which measured blood velocity in the descending aorta. The device did not measure the descending aortic diameter which was estimated using nomogram (a nomogram is the table of estimated values of the aortic diameter which is calculated by comparing patients weight, height, age and postmortem aortic diameter). It has been
suggested that these nomograms could be a potential error source in CO measurement\textsuperscript{29,30}.

One of the most recent transesophageal Doppler (TED) CO monitoring devices is the Hemosonic 100\textsuperscript{TM} (Arrow International). It measures blood velocity in the descending aorta by using a 5 MHz Doppler transducer and records descending aortic diameter by using an M-mode ultrasound transducer.

The transesophageal probe is a 20 French, 60 cm long flexible shaft. The probe is covered with an ultrasound transparent jacket filled with acoustic gel. The jacket protects the probe, ensures the proper transmission of the ultrasound to the tissues, and avoids esophageal mucosal injury caused by the rotation of the probe. An articulated arm is attached to the surgery table and holds the probe in its proper position. Two ultrasound transducers are located towards the end of the probe, and adjacent to the 5 cm long flexible silicone tip. Aortic blood velocity is measured with the pulsed Doppler ultrasound transducer which is at the same time the receiver. The probe has a rotatable inner part attached to the transducers and an outer part that is fixed. By using the probe handle the inner part can be rotated to position the transducers without moving the outer part or the jacket.

The echo-Doppler screen displays blood velocity from the Doppler transducer and the M-mode aortic tracing. It guides the user in obtaining the optimal probe position. The monitoring screen displays hemodynamic parameters of the patient.

Aortic diameter is measured by the M-mode transducer. The emitted ultrasound beam is perpendicular to the central probe axis. Because of the incident
beam is high collimation, choice of 10 MHz frequency, and size of the receiver; angular scattering from the aorta occurs in a very narrow spatial angle. If the probe and the aorta are correctly aligned (parallel to each other) the reflected ultrasound beam from the proximal and distal walls are detected by the receiver. When the incident beam is directed obliquely across the aorta only the signal reflected from the proximal aortic wall is detected by the receiver\textsuperscript{34}.

The pulsed Doppler ultrasound transducer measures the blood velocity in the descending aorta using a 5 MHz widely planar beam that bisects the aorta at a 60 degree angle. The device measures the Doppler frequency shift produced by the moving blood cells and converts it onto the spatially averaged blood velocity in the entire aortic cross section. The ultrasound beam “range gated” to improve the accuracy of the received signal\textsuperscript{34}.

Besides ABF and CO the machine also provides numerical information about: PV, Acc, left ventricular ejection time (LVETi) and TSVR\textsuperscript{35}. The HemoSonic100\textsuperscript{TM} might be a promising device that could be used on everyday basis in human critical care medicine as well as in veterinary critical care medicine and anesthesia. It is a nontraumatic technique that provides continuous, real time hemodynamic monitoring. Since it also measures or calculates preload, afterload and contractility parameters it provides the clinician with to rapidly interpret and precisely manage changes in the blood flow.

In the past few years, the research of esophageal Doppler systems has been intensified, especially in human medicine where the CO monitoring is integral part of intensive care medicine. Transesophageal Doppler (TED) recordings were usually
performed simultaneously with TD measurements. Although there are reports which indicated a high correlation between the two methods\textsuperscript{36,37}, other studies did not\textsuperscript{29,30}. A low correlation has been reported in certain surgical procedures such as aortic reconstructive surgery\textsuperscript{39}, cardiac surgery\textsuperscript{38} or liver transplantation surgery\textsuperscript{30}. There have been also reports that some pharmacological interventions, like epidural pain management, might interfere with the accuracy of the ultrasound monitoring procedure\textsuperscript{40} leading to a low correlation between TD and TED.

The TED has not been extensively examined for veterinary purposes. Wong at al. (1991) reported that TED correlated poor with TD after changes in preload, afterload and contractility in pigs\textsuperscript{29}. Young al. reported that after dopexamine hydrochloride infusion in the horses, the Doppler signal was not adequate and the authors hypothesized that lack of the quality in Doppler signal, might be responsible for the inaccurate CO measurements\textsuperscript{27}.

While TD has not been accepted in veterinary medicine as a standard procedure due to the relatively high cost of the equipment, invasive nature of procedure and personal training requirements, the non-invasive Doppler techniques might offer less complicated and still reliable methods for CO estimation in critical care veterinary medicine and anesthesiology.

\textit{b) Transthoracic approach}

While literature data implicated high correlation between transthoracic ultrasound techniques and invasive methods\textsuperscript{25}, the major disadvantages of this method are the high cost of the equipment, a need for competent and trained
personnel and relatively slow data acquisition since the proper positioning of the probe is essential for the reliable readings of the CO. These disadvantages are major limiting factors for the use of this technique, especially during emergency and surgical conditions where information has to be obtained fast and accurate.

While different methods have been described for measurement of CO, it is not clear which particular method would be the most suitable for the clinical use in veterinary medicine. The major advantage of the invasive methods is accuracy in the estimation of the cardiac output. However, the invasive nature of the procedure, is the major limiting factor for the widespread use of these methods. Doppler based ultrasound machines are characterized by non-invasiveness and relatively good accuracy in CO measurement in human patients. While these machines, are primarily designed and adjusted to the human anatomical and physiological characteristics, they might be effective tools for the evaluation of animal patients during critical conditions. Due to the anatomical differences between human and veterinary patients it is essential to thoroughly investigate, whether these techniques can be reliably used in different animal species.
References:


CHAPTER 2. MEASUREMENT OF CARDIAC OUTPUT BY TRANSSESOPHAGEAL DOPPLER ULTRASONOGRAPHY IN ANESTHETIZED DOGS - COMPARISON WITH THERMODILUTION

A paper to be submitted to Veterinary Anesthesia and Analgesia

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Abstract

Objective: To compare cardiac outputs (CO) measured by a transesophageal Doppler ultrasound technique (TED, Hemosonic 100™, Arrow Int) and CO measured by thermodilution (TD) in anesthetized dogs.

Design: Interventional studies

Settings: Veterinary Teaching Laboratory– Iowa State University

Animals: The study included 10 canines weighing from 18.5 kg to 32.5 kg. Set criteria for inclusion were adequate body size of the dogs for placement of the esophageal probe (body weight >18.5 kg) and stable anesthesia maintenance period.

Interventions: Simultaneous TED and TD measurements of CO were obtained during initial baseline period. The baseline CO was then altered by constant rate intravenous infusion of dobutamine, dopamine and norepinephrine; and by caudal vena cava occlusion.
**Results:** Each measurement of CO allowed a comparison of TED and TD values. Forty-nine CO paired comparisons were made with the CO ranging from 0.73 l/min to 10.9 l/min (obtained by TD). Simple linear regression was used to determine the correlation between the two techniques ($r^2=0.53$). Bland and Altman statistical method was used for assessing agreement between the two methods. The difference between the TD and TED was 0.82 l/min (bias) and SD was 1.63 l/min. At baseline and low CO levels (caudal vena cava occlusion) the correlation coefficient ($r^2$) was 0.77 and at high CO levels (dobutamine, dopamine and norepinephrine infusions) the correlation coefficient ($r^2$) was 0.45.

**Conclusion:** The TED might be a useful method for detecting low CO trends and aid in determining the cause of hypotension.

**Keywords:** cardiac output, Doppler ultrasound, thermodilution, dog.
INTRODUCTION:

The practice of anesthesiology involves providing support for critically ill patients undergoing surgery. This requires accurate monitoring of parameters which are capable of predicting oxygen delivery to the tissues. Unfortunately, critically ill patients in almost all situations have significantly compromised pulmonary and cardiovascular function which anesthetic drugs may compromise even further. Therefore, monitoring these patients is a crucial goal and one of the biggest challenges in veterinary anesthesia practice. An accurate, non-invasive method for measuring cardiac output (CO) would be extremely beneficial for the proper evaluation of the cardiovascular function in critically ill patients.

In human medicine, CO monitoring has become an integral part of cardiovascular monitoring in critically ill patients undergoing general anesthesia. Thermodilution (TD) is the most commonly employed method of CO monitoring but, there are some well recognized limitations regarding the use of the technique: 1) pulmonary artery catheterization requires time and participation of experienced personnel to position the catheter, 2) it provides only intermittent hemodynamic information, 3) data could be misinterpreted, 4) the cost is not negligible, and 5) TD has been associated with increased mortality or morbidity. In veterinary medicine TD is rarely used in clinical settings because of its invasive nature and cost and it has been mainly used in the research purposes.

Transesophageal Doppler ultrasonography (TED) is a minimally invasive technique for measuring blood flow in the descending aorta based on the Doppler effect. The Doppler effect is based on a change in frequency or wave length of
ultrasound caused by the motion of a wave source, receiver, or reflector. In the case where the CO is to be determined, the moving objects are blood elements. Ultrasound waves are reflected with a different wave length from the moving blood cells. This change in frequency or wave length is used to calculate the velocity of blood flow and is basic principle behind all Doppler techniques for the measurement of CO regardless of the type of machine or position of the probe. The TED, with the advantage of being relatively easy to perform and continuous CO monitor might offer an alternative to TD$^{9,10,11}$.

Recently, Arrow International has marketed in Europe and North America an TED ultrasound based system for monitoring CO (Hemosonic 100™).

The purpose of this study was to compare CO values obtained by TED with those obtained by TD in anesthetized dogs and evaluate the potential usefulness of TED for obtaining CO measurements during conditions characterized by low or high CO values.

**MATERIALS AND METHODS:**

All animal studies were conducted in accordance with the Guiding Principles in the Care and Use of Animals (DHEW Publication, NIH 80-23) and procedures were approved by the Iowa State University Committee on Animal Care. Ten mixed breed dogs were used in the study. All dogs were given a preanesthetic medication of acepromazine (0.1 mg/kg, IM). Anesthetic induction was accomplished by use of thiopental (10 mg/kg, IV) and maintenance with isoflurane. End-tidal isoflurane and carbon dioxide (CO$_2$) concentrations were maintained at 1.3% and 35-45 mmHg,
respectively. Eight of the ten dogs were studied following a veterinary student surgical laboratory.

Instrumentation and monitoring

Systolic, diastolic and mean blood pressures were monitored by catheterizing the dorsal metatarsal artery. The arterial catheter was connected to a pressure transducer (Tru Wave, Baxter) and monitor (Passport, Datascope corporation). An electrocardiogram (ECG) was used to assess heart rate (HR) and rhythm. Pulse oximetry was used to measure pulse rate and arterial hemoglobin oxygen saturation. A capnometer was used for measuring end-expiratory and inspiratory CO₂ concentrations. Normocapnia (end-tidal CO₂ from 35 to 45 mmHg) was maintained by mechanical ventilation (Hallowell engineering, manufacturing corporation). Body temperature was maintained between 95-100 F with circulating warm water pads (Gaymar) and forced warm air (Bair Hugger, Augustin). A 6 French, 80 cm, balloon tipped occlusion catheter (Fogarty, Edwards Lifesciences) was inserted through the femoral vein and advanced to the thoracic portion of the caudal vena cava. The balloon was inflated with air to produce caudal vena cava occlusion. A 7 French, 4 lumen, 110 cm balloon tipped thermodilution catheter (Arrow International) was inserted through the jugular vein and advanced to the level of the pulmonary artery (guided by pressure wave analysis).

The TED probe was covered with a disposable gel filled sheath (jacket), lubricated, and inserted into the esophagus to the level of the seventh or eighth intercostal space. The probe was then rotated until the best echo and Doppler signals were found. The probe insertion depth and orientation were checked before
each recording of data such that both the proximal and distal aortic walls were visualized (with maximum aortic diameter) and an appropriate velocity curve from the pulsed Doppler transducer appeared on the monitor.

**Measurement of CO**

The TD CO measurement procedure was performed by injecting 5 cc of cold 5% dextrose in water through the proximal port (right atrium) of the pulmonary artery catheter in the right atrium. The catheter's thermistor was connected to a computer (COM-2, Baxter Healthcare corporation) which converted the resultant blood temperature change into the CO. Syringes were prefilled with 5% dextrose and kept in an ice bath for at least 6 hours prior to each procedure. All TD measurements were performed at the end of expiration by arresting the ventilator. Each TD CO measurement was an average of 3 consecutive values which were obtained with a difference less than 10%. The mean of TD CO measurements were used for comparison with the mean of three simultaneously obtained TED measurements.

**Experimental protocol:**

During the initial baseline period no pharmacological or mechanical interventions were made. The CO was then altered by randomly administering the following treatments: dobutamine (10 µg/kg/min), dopamine (10 µg/kg/min), norepinephrine (10 µg/kg/min), and caudal vena cava (CVC) occlusion. The baseline CO was always performed at the beginning of each experiment followed by the treatments administered randomly to each dog. No attempt was made to ensure that the CO was identical for each treatment for each dog. Measurements were only obtained when the dogs were hemodynamically stable following application of the
treatment. Each treatment was continued for at least 10 minutes to achieve stable CO values\textsuperscript{12}. Hemodynamic and respiratory variables were recorded to document stability during the data collection.

**Transesophageal Doppler monitoring system description**

The Hemosonic 100\textsuperscript{TM} (*Arrow International*) consists of a main console, connection cable, transesophageal probe, probe jacket and articulated arm with the probe holder. The main console contains electrical hardware, control keys, and connectors. Three screens may be displayed on the main console. The first screen displays instructions for the user. The second is echo-Doppler screen which displays blood velocity from the Doppler transducer and the M-mode aortic tracing. It guides the user in obtaining the optimal probe position. The third monitoring screen displays hemodynamic parameters of the patient. A connection cable is used to attach the probe to the main console. The transesophageal probe is a 20 French, 60 cm long flexible shaft which is covered with an ultrasound transparent jacket filled with acoustic gel. The jacket protects the probe, ensures the proper transmission of the ultrasound to the tissues, and avoids esophageal mucosal injury caused by the rotation of the probe. The articulated arm is attached to the surgery table and holds the probe in its proper position. Two ultrasound transducers are located towards the end of the probe (Fig. 1) and adjacent to the 5 cm long flexible silicone tip. Aortic diameter is measured by an M-mode transducer and the aortic blood velocity is measured with a pulsed Doppler ultrasound transducer. The probe has an inner part where the transducers are located and outer part that is fixed. By
using the probe handle the inner part can be rotated to position the transducers without moving the outer part or the jacket.

**Measurements of diameter and blood velocity in the descending aorta**

The M-mode ultrasound transducer was used to measure the descending aortic diameter. The emitted ultrasound beam is perpendicular to the central probe axis. Because of the incident beam's high collimation, 10 MHz frequency, and size of the receiver, angular scattering from the aorta occurs in a very narrow spatial angle. When the probe and the aorta are correctly aligned (parallel to each other) the reflected ultrasound beam from the proximal and distal walls are detected by the receiver (Fig.2A). If the incident beam is directed obliquely across the aorta (Fig. 2B) only the signal reflected from the proximal aortic wall is detected by the receiver\textsuperscript{13}.

The pulsed Doppler ultrasound transducer measures the blood velocity in the descending aorta. It produces a 5 MHz widely planar beam that bisects the aorta at a 60 degree angle. The device measures the Doppler frequency shift produced by the moving blood cells which provides a measurement of the spatially averaged blood velocity in the entire aortic cross section (Fig. 1) and gates the range of the received signal\textsuperscript{13}.

**STATISTICAL ANALYSES**

Correlation between the two techniques was determined using simple linear regression analysis. A p value smaller than 0.05 was considered statistically significant. Simple linear regression was also performed separately with data
obtained during the baseline and vena cava occlusion periods (referred to as low CO levels) and dobutamine, dopamine and norepinephrine infusion periods (referred to as high CO levels). Bland and Altman analysis was used to assess agreement and explore for systematic and random errors. The bias (mean difference) represents the systematic error between the two methods. The SD of the bias represents the random error or variability between the different methods. Mean difference +/- 2SD is known as the “limits of agreement”. Since all dogs underwent more than one CO measurement the variations between two time points in TD and TED were compared using two way analysis of variance (ANOVA) for repeated measurement with Tukey-Kremor post-test analysis to confirm that the difference between baseline level and other 4 levels was statistically significant.

RESULTS

The TD and TED CO pairs were compared in each dog and treatment. A total of fifty CO paired comparisons were possible. After exclusion of one CO pair during dobutamine infusion in one dog (marked tachycardia), forty nine CO paired observations were used for the statistical analyses. There were ten baseline, nine dobutamine, ten dopamine, ten norepinephrine and ten caudal vena cava occlusion measurements. The mean values +/- SEM for all five CO levels measured by TD and TED are presented in table 1. Transesophageal probe placement was easily accomplished in each dog. An adequate M-mode and Doppler signals were found within a few minutes. Cardiac output ranged from 0.73 l/min to 10.9 l/min when measured using TD, and from 1.25 to 6 l/min when measured by TED. A significant
correlation between TED and TD measurements was present during the baseline and caudal vena cava occlusion levels (n=20, \( r^2=0.77, p<.0001 \), Fig. 3A). A significant correlation was no longer present during dobutamine, dopamine and norepinephrine interventions (n=29, \( r^2=0.45, p<.0001 \), Fig. 3B). In addition, when all measurements were included the correlation was not significant (n=49, \( r^2=0.53, p<.0001 \), Fig 3C).

The Bland-Altman analysis included all data. The mean difference between TD and TED measurements (bias) was 0.82 l/min, 1 SD was 1.63 l/min and the limit of agreement was –2.44 to 4.08 l/min (Fig. 4). The ANOVA for repeated measurements with Tukey-Kremor post-test analysis confirmed significant difference between baseline versus dobutamine (\( p<0.001 \)), dopamine (\( p<0.01 \)) and norepinephrine (\( p<0.05 \)) CO levels. In addition, the same test confirmed a significant difference between caudal vena cava occlusion vs the previous treatment values (\( p< 0.001 \)).

**DISCUSSION**

The statistical analysis revealed a significant increase in the CO when positive inotropic agents were used and a significant decrease of the CO with CVC occlusion. There was a weak correlation between TED and TD techniques when dobutamine, dopamine and norepinephrine were used (\( r^2=0.45 \)). When the CVC occlusion was used to decrease CO, the correlation between two the techniques was reasonably good (\( r^2=0.77 \)). However, when all paired data were combined the general correlation analysis coefficient was weak (\( r^2=0.53 \)). The Bland and Altman
analysis revealed that the systemic error (bias) between two techniques was 0.82 l/min. This indicate that TED measurements can differ from TD measurements for 0.82 l/min at any time. Since the Hemosonic 100TM was calibrated to calculate CO from the ABF in the descending aorta in humans, it is possible that this has influenced the magnitude of the bias. However 1 SD was large (1.63 l/min) and limits of agreement were large ranging from -2.44 l/min to 4.08 l/min. Observing the Bland-Altman plot, there is an obvious increase in scattering as the CO increases indicating that there is a less agreement between two techniques in higher CO levels. Previously published data regarding the accuracy of CO measurements obtained by TED are conflicting. Wong and colleagues\textsuperscript{14} used transient time ultrasound (TTU) as a reference method in pigs. The agreement between TED and TTU was good in the decreased preload group induced by bleeding, however weak agreement was observed between the two techniques in the increased contractility group when dobutamine infusion was used. In the study where various degrees of cardiac tamponade in pigs were used to decrease CO, the correlation between TD and TED was high ($r^2\approx0.89$)\textsuperscript{9}. A study on humans receiving liver transplants revealed an inconsistent difference between TD and TED\textsuperscript{15}. However, other studies on human patients observed a good correlation between the two techniques when dobutamine\textsuperscript{10,16} and fluid therapy\textsuperscript{17} were used. Young and colleagues reported\textsuperscript{18} reported that tranesophageal echocardiography can provide an alternative for TD in anesthetized horses.

The assessment of CO by TED offers several advantages over TD but the determination of CO by the Hemosonic100\textsuperscript{TM} is based on several assumptions which
may cause inaccuracies. The first assumption is that the aorta and esophageal probe are positioned nearby and parallel to each other. The Hemosonic 100™ uses the M-mode ultrasound imaging of the aortic walls and clear visualization of the proximal and distal aortic walls on the monitoring screen is the confirmation of proper probe positioning. During this study, the probe was repositioned prior to each CO measurement, in an attempt to improve the M-mode signal. A computed tomography scan of one dog with the TED probe properly positioned revealed that the probe was nearby desired parallel to the aorta (Fig 5). In humans a satisfactory M-mode signal is usually obtained when the transducer is positioned at the level of the third intercostal space. In this study, the best M-mode signal was obtained when the transducer was positioned at the level of the seventh intercostal space. The exact position of the probe was confirmed on postmortem examination of three dogs.

The second assumption is that the blood flow in the descending aorta is laminar since the Doppler transducer averages the blood velocity over the entire cross section during the ejection phase. It's not known whether positive inotropic drugs induce turbulent blood flow in dogs. However, an irregular shape of the Doppler signals in this study (Fig 6) closely resembles changes observed in dogs where methoxamine caused turbulent blood flow. In addition, during dobutamine, dopamine and norepinephrine infusions, the down-stroke of Doppler velocity trace became notched in the most dogs. Young and colleagues have reported the similar finding in horses during dopexamine hydrochloride infusions.

The third assumption is that the distribution of ascending aortic blood flow remains always the same since CO is calculated from the ABF under assumption
that 70% of CO is distributed in the descending aorta and 30% of CO is distributed in the brachiocephalic trunk and left subclavian artery. However, it has been reported that under the sympathetic and vagal stimpulation in dogs this ratio changes. In addition, the study where the different cathecholamines were used in dogs, CO distribution ratio was also changed.

CONCLUSION

The TED as a method for CO measurement that may have value in canine patients with compromised cardiovascular parameters and decreased CO. This study demonstrated that TED has a reasonably good correlation with TD during low CO conditions and it is hypothesize that TED might be a useful non-invasive monitoring technique in similar clinical conditions. However, in situations, where blood flow might have turbulent characteristics, the validity and accuracy of this method does not appear to be sufficient for clinical use in dogs.

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Figure 1. The pulsed Doppler ultrasound transducer measures the blood velocity in the descending aorta with the 5 MHz widely planar beam that bisects the aorta at a 60 degree angle. The M-mode transducer measures descending aortic diameter using 10 MHz, highly collimated beam.
Figure 2. A) The incident beam is directed obliquely across the aorta and only the signal reflected from the proximal aortic wall is detected by the receiver. B) If the probe and the aorta are correctly aligned (parallel to each other) the reflected ultrasound beam from both the proximal and distal walls are detected by the receiver.
Figure 3. A) Significant correlation between TED and TD measurements was present during the baseline and caudal vena cava occlusion levels (n=20, $r^2=0.77$, $p<.0001$). B) The significant correlation was no longer present during dobutamine, dopamine and norepinephrine interventions (n=29, $r^2=0.45$, $p<.0001$). C) The correlation was not significant for all measurements (n=49, $r^2=0.53$, $p<.0001$, Fig 3c).
Figure 4. The Bland-Altman analysis. The mean difference between TD and TED measurements (bias) was 0.82 l/min, 1 SD was 1.63 l/min and the limit of agreement was −2.44 to 4.08 l/min.
Figure 5. A computed tomography scan of an anesthetized dorsally recumbent dog showing the TED probe positioned nearby and parallel to the aorta while baseline recordings are being made.
Figure 6. The irregular shape of Doppler signals was detected when positive inotropes (in this picture - dobutamine) were used.
<table>
<thead>
<tr>
<th></th>
<th>TD (l/min)</th>
<th>TED (l/min)</th>
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<tbody>
<tr>
<td>Baseline (mean±SEM)</td>
<td>2.73±0.38</td>
<td>2.43±0.25</td>
</tr>
<tr>
<td>Dobutamine (mean±SEM)</td>
<td>5.52±0.92</td>
<td>3.13±0.26</td>
</tr>
<tr>
<td>Dopamine (mean±SEM)</td>
<td>4.73±0.54</td>
<td>3.59±0.31</td>
</tr>
<tr>
<td>Norepinephrine (mean±SEM)</td>
<td>4.39±0.49</td>
<td>2.91±0.27</td>
</tr>
<tr>
<td>CVC occlusion (mean±SEM)</td>
<td>1.58±0.25</td>
<td>2.12±0.21</td>
</tr>
</tbody>
</table>

**Table 1.** The mean values +/- SEM for all tested CO levels measured by TD and TED and ANOVA for repeated measurements results. Values significantly different from baseline- *** (p<0.001), ** (p<0.01), * (p<0.05). Values significantly different from the previous treatment- +++ (p<0.001).
CHAPTER 3. GENERAL CONCLUSIONS

General discussion

The purpose of this study was to compare CO values obtained by TED with CO values obtained by TD in healthy dogs and evaluate potential usefulness of the TED as a non-invasive method for CO measurements during low and high CO conditions.

While different methods have been described for CO measurement it is still not clear which particular method would be the most suitable for frequent use in veterinary medicine. The major advantage of invasive methods is accuracy in the estimation of the CO. However, the invasive nature of the procedure is the major limiting factor for the widespread use of these methods. The Doppler based ultrasound machines are characterized by non-invasiveness and good accuracy in the measurement of CO in human patients. Due to anatomical differences between human and veterinary patients, this project was designated to investigate, whether TED can be reliably used in dogs.
Ten healthy dogs were used in the experiment. Each dog received a random application of treatments to alter CO values. Dobutamine, dopamine and norepinephrine were used as positive inotropic agents to increase CO, while CVC occlusion was used to decrease venous return to the heart and subsequently decrease CO.

Cardiac output in our study ranged from 0.73 l/min to 10.9 l/min when measured using thermodilution, and from 1.25 to 6 l/min when measured by TED. Significant correlation between TED and TD measurements was present during the baseline and caudal vena cava occlusion levels (n=20, r=0.77, p< .0001). However, the correlation was no longer significant during dobutamine, dopamine and norepinephrine interventions (n=29, r=0.45, p<.0001). When all paired data were combined the general correlation analysis coefficient was weak (r²=0.53).

This study demonstrated that TED has a reasonably good correlation with TD during low CO conditions and it is hypothesized that TED might be a useful non-invasive monitoring technique in similar clinical conditions. However, in situations, where blood flow might have turbulent characteristics, the validity and accuracy of this method does not appear to be sufficient for the regular clinical use in dogs.

Further directions
This experiment revealed a potential for the use of TED for CO monitoring in healthy dogs with experimentally induced low CO. To validate the utility of the method, it would be essential to perform recordings in real patients who suffer from serious malfunction of the cardiovascular and/or respiratory system. Furthermore, it would
be very important to correlate outcome of therapeutic strategies in critical patients whose therapy was guided by TED parameters and compare survival rate with patients which received therapy without precise estimation of the CO values. The validity and justification of the method can be achieved only when a cohort of patients is analyzed and benefit of the procedure is proved. Until that kind of evidence is available, the recommendation for the frequent use of TED in veterinary anesthesia and critical care can not be given.
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