

Guro Strøm Solli

Effects of increased exercise intensity on the heart's stroke volume in elite female cross country skiers

Master's Thesis Exercise Physiology and Sport Sciences
Trondheim, June 2010

NTNU
Norwegian University of Science and Technology
Faculty of Medicine
Department of Circulation and Medical Imaging

CONTENT

ABBREVIATIONS.....	3
ABSTRACT	4
INTRODUCTION	5
Plateau.....	5
Increase in SV to VO_{2max}	6
The SV response in female subjects	7
Endurance training	8
Gender differences.....	9
Reliability and Validity of the SV test	10
The aim of present study.....	12
Hypothesis	12
METHODS	13
Subjects	13
Testing apparatus	13
<i>Treadmill</i>	13
VO_{2max}	13
<i>Heart rate (HR)</i>	14
<i>Cardiac output and stroke volume</i>	14
Testing procedure	15
VO_{2max}	15
<i>Cardiac output and Stroke volume</i>	15
Exercise intensities	16
Statistical analysis.....	16
RESULTS.....	17
DISCUSSION	19
Stroke volume response to increased exercise intensity.....	19
Plateau in SV from 40% to 80% of VO_{2max}	20
The increase in SV from 40% to 100% of VO_{2max}	21
SV_{max}	22
Cardiac output.....	23
VO_{2max}	23
CONCLUSIONS	24
Practical application of the study.....	24

ABBREVIATIONS

BV - Blood volume

C₂H₂ – Acetylene

CH₄ - Methane

CO - Carbon Monoxide

CO₂ - Carbon dioxide

ET – Endurance trained

HR - Heart Rate

HR_{max} - Maximum Heart Rate

N₂ - Nitrogen

O₂ - Oxygen

Q - Cardiac Output

Q_{max} - Maximum Cardiac Output

SB - Single Breath Acetylene Method

SD - Standard Deviation

SEM – Standard error of Mean

SPSS - Statistical Package for Social Sciences

SV - Stroke Volume

SV_{max} - Maximal Stroke Volume

V - Coefficient of Variation

VO₂ - Oxygen Consumption

VO_{2max} - Maximal Oxygen Consumption

ABSTRACT

Purpose: Previous research has shown that endurance trained (ET) males increase stroke volume (SV) progressively with increasing exercise intensity up to maximal oxygen uptake (VO_{2max}). However, few investigations have included ET female subjects. The purpose of this study was to investigate the SV response to increased exercise intensity in ET women.

Method: Thirteen elite female cross country skiers were tested for VO_{2max} using the Metamax II. Cardiac output (Q) was measured at rest, 40%, 60%, 80% and 100 % of VO_{2max} , using the single breath acetylene rebreathing method. SV was calculated by dividing Q with HR. **Results:** Mean VO_{2max} was $67.1 \pm 6.1 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, $4.072 \pm 0.219 \text{ L}\cdot\text{min}^{-1}$. Mean SV_{rest} was $72.3 \pm 12.6 \text{ mL}\cdot\text{beat}^{-1}$ and mean SV_{max} was $129.1 \pm 16.3 \text{ mL}\cdot\text{beat}^{-1}$. The SV increased from rest to 40% of VO_{2max} , plateaued from 40-80 % of VO_{2max} and then increased from 80-100% of VO_{2max} ($P < 0.05$). Q_{rest} was $6.6 \pm 0.6 \text{ L}\cdot\text{min}^{-1}$ and Q_{max} was $23.5 \pm 2.5 \text{ L}\cdot\text{min}^{-1}$. Q increased progressively with increasing exercise intensity up to VO_{2max} ($P < 0.05$). **Conclusion:** The SV of the present elite female cross country skiers increased from rest to 40% of VO_{2max} , plateaued from 40-80 % of VO_{2max} and then made a secondary increase from 80-100% of VO_{2max} . The hypothesis of a progressive increase in SV with increased exercise intensity, as observed in ET men, was thus rejected.

INTRODUCTION

Research investigating the heart's stroke volume (SV) response to increased exercise intensity in humans has shown inconsistent results. Vella and Roberg (2005) reported 4 main types of SV response in the literature; Plateau, plateau with a drop, plateau with a secondary increase and progressive increase (Vella and Robergs 2005). Historically the main discussion has been whether the SV plateaus at 40-50% of maximal oxygen uptake (VO_{2max}) or continues to increase with elevated exercise intensity. Research suggests that male endurance athletes in particular have the capacity to increase SV progressively to the point of maximal exercise. A lack of research including endurance trained (ET) females makes it uncertain whether the same is true for women.

Plateau

Åstrand et al. (1964) reported that the maximum SV was reached at 40% of VO_{2max} and maintained to VO_{2max} in sedentary men and women, 20-31 years of age. This was also found by Bevegard et al. (1963) investigating endurance trained (ET) young men, and further supported by Grimby et al. (1966). Based on these studies, the theory of a SV plateau at 40-50% of VO_{2max} became an accepted theory and was presented in most textbooks. The theory was supported by the fact that elevated HR leads to a decreased time for diastolic filling (Higginbotham et al. 1986; Rubal et al. 1986).

Several recent investigators have reported a plateau response in SV. However, most of the studies reporting a plateau in SV include participants with VO_{2max} suggesting that they are average to moderately active (Bevegard et al. 1963; Åstrand et al. 1964; Higginbotham et al. 1986; Spina et al. 1992; Gledhill et al. 1994; McLaren et al. 1997; Proctor et al. 1998; Zhou et al. 2001) or untrained (Hagberg et al. 1985; Higginbotham et al. 1986; Sullivan et al. 1991; McLaren et al. 1997). However, a plateau in SV has also been observed in ET men with mean $VO_{2max} > 70 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (Hagberg et al. 1985; Rivera et al. 1989; Zhou et al. 2001).

Increase in SV to VO_{2max}

It is questionable why the theory of a SV plateau became so widely accepted, when the individual data of both Åstrand et al. (1964) and Grimby et al. (1966) showed that 11 and 4 of the participants in these studies reached their highest SV during maximal exercise. In addition Chapman already in 1960 reported that the mean SV of 26 healthy men increased progressively during incremental exercise. This was supported by Ekblom and Hermansen (1968) that found a progressive increase in SV from 40% of VO_{2max} to maximal exercise in eight elite (mean VO_{2max} 74.6 ml·kg⁻¹·min⁻¹) and five regional level (mean VO_{2max} 66.0 ml·kg⁻¹·min⁻¹) endurance athletes.

More recent investigations have identified a difference in the SV response to increased exercise intensity in ET and untrained subjects. Gledhill and coworkers (1994) observed that the SV in competitive male endurance cyclists (mean VO_{2max} 69 ml·kg⁻¹·min⁻¹) increases over the heart rate (HR) range of 90 to 190 beats per min (bpm). However, the SV in normally active males (mean VO_{2max} 44 ml·kg⁻¹·min⁻¹), did plateau at an average HR of 120 bpm. This was supported by Zhou et al. (2001) reporting a different SV response in three levels of male distance runners. The groups were elite (mean VO_{2max} 84 ml·kg⁻¹·min⁻¹), distance runners (mean VO_{2max} 72 ml·kg⁻¹·min⁻¹) and untrained (mean VO_{2max} 49 ml·kg⁻¹·min⁻¹). The SV of the untrained and distance runners did plateau at about 40% of VO_{2max} , but in the elite distance runners, the SV continued to increase throughout exercise to VO_{2max} . The same difference in SV response was observed by Crawford et al. (1985) investigating competitive and non-competitive runners.

Several other investigators have supported the finding that male ET subjects have the ability to increase SV to VO_{2max} (Vanfraechem 1979; Ahmad and Dubiel 1990; Krip et al. 1997; Wiebe et al. 1998; Warburton et al. 1999; Warburton et al. 2002; Ramola 2008). However, Krip and colleagues (1997) reported a progressive increase in SV in untrained male subjects (mean VO_{2max} 42 ml·kg⁻¹·min⁻¹) during cycle exercise with increased intensity to exhaustion. The theory of a plateau in SV still has a fair amount of evidence behind it, but mainly from untrained subjects. Trained subjects data seems to suggest an increase in SV up to VO_{2max} . But in all cases there is data to contradict.

The SV response in female subjects

Most of the studies investigating the SV response in women have reported a plateau or a decline in SV when exercise intensity exceeds 50% of VO_{2max} (Åstrand et al. 1964; Sullivan et al. 1991; Ogawa et al. 1992; Proctor et al. 1998). Still, there is evidence that women also have the ability to increase SV with exercise intensity above 50% of VO_{2max} . Ferguson et al. (2000) found that the SV in ET females (mean VO_{2max} 64 ml·kg⁻¹·min⁻¹) continued to increase throughout incremental work rates up to maximum, whereas the SV in the active women (mean VO_{2max} 42 ml·kg⁻¹·min⁻¹) increased from rest to submaximal HR then plateaued and made a secondary increase to HR_{max}. Wiebe et al. (1999) investigated the SV response in ET women divided into four age groups, 20-29, 40-45, 49-54 and 58-63 years, matched for lean body mass. The SV increased progressively throughout incremental exercise to VO_{2max} in all groups. Overall there are few studies investigating the SV response with increased exercise intensity in female subjects, particularly highly ET women (table 1).

Table 1: Summary of the literature on the stroke volume response to increased exercise intensity including female subjects

References	N	Age (years)	Training status	VO_{2max} (ml·kg ⁻¹ ·min ⁻¹)	SV_{max} (ml·beat ⁻¹)	SV response to increased exercise intensity
Ferguson et al.	7	18-30	ET	64.3	121	Progressive increase to VO_{2max}
Ferguson et al.	7	18-30	MA	42.1	90	Plateau with a secondary increase
Wiebe et al.	23	20-63	ET	40-70	104-125	Progressive increase to VO_{2max}
Proctor et al.	6	27	ET	45.6	-	Plateau
Proctor et al.	8	61	ET	35.1	-	Decline with increased intensity from 70-90% of VO_{2max}
Åstrand et al.	11	20-31	-	41.4	100	Plateau
Sullivan et al.	27	20-63	-	28.4	-	Plateau
Ogawa et al.	14	23	SED	37.0	80	Decline with increased intensity from 50-100% of VO_{2max}
Ogawa et al.	13	26	ET	52.1	102	Decline with increased intensity from 50-100% of VO_{2max}
Ogawa et al.	14	64	SED	22.2	74	Decline with increased intensity from 50-100% of VO_{2max}
Ogawa et al.	13	57	ET	35.3	85	Decline with increased intensity from 50-100% of VO_{2max}

Data are presented as mean or range. VO_{2max} ; Maximal oxygen uptake, SV_{max} ; Maximal stroke volume, SV; Stroke volume, ET; Endurance trained, MA; Moderately active, SED; Sedentary.

Endurance training

Scientific research has reported a difference in the SV response between ET and untrained individuals (Crawford et al. 1985; Gledhill et al. 1994; Ferguson et al. 2001; Zhou et al. 2001). Maximal stroke volume (SV_{\max}) is also observed to be higher in ET individuals, compared to less trained subjects (Gledhill et al. 1994; Krip et al. 1997; Ferguson et al. 2001; Zhou et al. 2001). This suggests that endurance training may be of vital importance in determining the SV response to increased exercise intensity.

A unique rise of the SV in endurance athletes compared with untrained would need to be achieved by a progressive rise in ventricular preload and/or augmented myocardial contractility during exercise (Rowland 2009). Current research has reported both enhanced diastolic filling (Gledhill et al. 1994; Krip et al. 1997; Ferguson et al. 2001) and shorter diastolic filling times in ET individuals (Wolfe et al. 1978; Gledhill et al. 1994; Krip et al. 1997). Ferguson et al. (2001) discussed that the enhanced diastolic filling could be due to increases in blood volume (BV), a known adaptation to endurance training (Hopper et al. 1988; Stevenson et al. 1994; Mier et al. 1996). A larger BV leads to increased central venous pressure and an elevated venous return. This augments ventricular preload, which in turn enhances right ventricular filling and results in a higher end diastolic volume. This increases the response of the Frank-Starling mechanism, and the result is a more forceful contraction, which increases SV (Ekblom and Hermansen 1968; Kanstrup and Ekblom 1982; Hopper et al. 1988).

However, Martino and colleagues (2002) investigated a group of untrained men with exceptionally high $VO_{2\max}$ (mean $VO_{2\max}$ $65 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) and controls (mean $VO_{2\max}$ $46 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). BV, SV_{\max} and Q_{\max} were significantly higher in the group with the highest $VO_{2\max}$. Still, the same SV response (increase from rest to 50% of $VO_{2\max}$, plateau from 50% to 75% of $VO_{2\max}$, and increase from 75% to $VO_{2\max}$) was observed in both groups. Similarly Warburton et al. (1999) investigated the SV response during increased exercise intensity to $VO_{2\max}$ under two conditions: a 500mL BV expansion and a control condition. Both SV_{\max} and Q_{\max} were elevated after the BV enlargement, and the SV increased progressively to $VO_{2\max}$ under both conditions. These studies suggests that increased BV may be the cause of the high SV_{\max} and Q_{\max} values observed in ET subjects, but is not clear how much it affects the SV response to exercise.

Interestingly in the study by Zhou et al. (2001) an increase in SV from 40% to 100% of VO_{2max} was only observed in the elite group. An enlarged BV should be present in both the elite subjects and the well-trained university runners because the two groups had trained for years. This is suggesting that other factors, than increased BV, could be responsible for the different SV response observed between ET and sedentary subjects. Other cardiac adaptations observed in endurance athletes are enhanced ventricular emptying (Gledhill et al. 1994; Krip et al. 1997; Ferguson et al. 2001), longer ventricular ejection times (Wolfe et al. 1978; Gledhill et al. 1994; Krip et al. 1997), greater myocardial contractility (Vanfraechem 1979; Sullivan et al. 1991) and greater left ventricular diameter and mass (Finkelhor et al. 1986; Levy et al. 1993; Vinereanu et al. 2002; Hoogsteen et al. 2003). How these factors affect the SV with increased exercise intensity is not clear.

However, conflicting values question the importance of endurance training on the SV response to exercise. For example, a remarkable observation in the study of Zhou et al. (2001) was that although the distance runner's VO_{2max} averaged $72.1 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ($23 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ higher than the untrained group), they still exhibited a plateau in SV. In contrast, Krip et al. (1997) found a progressive increase in the SV of untrained men (mean VO_{2max} $42 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). Both studies included men at the same age, and used the acetylene rebreathing method to assess SV.

It is also important to note that there is a wide range in the VO_{2max} values between subjects reported as ET individuals. ET men at the same age vary from 55 to $84 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (Proctor et al. 1998; Zhou et al. 2001), while ET women of the same age can range between 46 to $64 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (Proctor et al. 1998; Ferguson et al. 2001). This makes it very difficult to compare studies and evaluate how much endurance training affects the SV response to exercise.

Gender differences

An interesting question is whether the SV response to exercise differs between men and women. Proctor et al (1998) investigated the influence of gender on cardiovascular responses to exercise in ET men and women (24-27 years) during cycle exercise at 40%, 70% and 90% of VO_{2max} . The women reached a plateau in SV at 40% of VO_{2max} which was

maintained throughout exercise. In contrast, the SV in men continued to increase progressively to 90% of VO_{2max} . However, the men had an average of $11 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ higher VO_{2max} than the woman.

Sullivan and coworkers (1991) compared men and women (20-63 years) using the SV index (SV per unit of body surface; $\text{mL}\cdot\text{m}_2^{-1}$). SV reached its maximum at 50% of VO_{2max} and remained unchanged through up to maximal exercise, in both men and women. There were no differences in SV index at rest or during exercise between groups. In addition, the increase in SV index from rest to exercise was similar in men and women. The authors concluded that, in healthy subjects, matched for body size and fitness level, gender was not an important determinant of the SV response to exercise (Sullivan et al. 1991).

Ogawa et al. (1992) reported a progressive decrease in the SV from 50% to VO_{2max} in both sedentary and ET men and women. However the SV in the women was lower at all workloads compared with the men, even after normalization to body weight. After normalization of SV to fat free mass, the gender difference was eliminated in sedentary subjects, but only reduced in the ET subjects. The authors concluded that the gender difference in the SV of the ET subjects was due to a greater percentage of body fat in women (Ogawa et al. 1992).

Submaximal Q is reported to be 5 to 10% lower in women compared to men. This is explained by the 10% lower hemoglobin concentration in women (McArdle et al. 2006 p. 358). This could also affect the SV response with increased exercise intensity in women. However, more research is needed to elucidate possible gender differences in the SV response to exercise.

Reliability and Validity of the SV test

SV is not measured directly but calculated by dividing Q by HR. The gold standard techniques for measuring Q are the direct Fick method, employing cardiac catheterization and the dye/thermo-dilution technique employing central venous catheterization (Ekblom and Hermansen 1968; Rerych et al. 1980; Crawford et al. 1985; Patel et al. 1986; Gledhill et al. 1994; Laszlo 2004). Because of the complicated procedures and the inherent risks of the instrumentation of these invasive measures, several indirect techniques have been

developed (Simmons and Shephard 1971). The most used indirect method for determining Q throughout incremental to maximum exercise is the acetylene rebreathing technique (Triebwasser et al. 1977; Smyth et al. 1984; Levine et al. 1991; Gledhill et al. 1994; Hsia et al. 1995; Helgerud et al. 2007; Jarvis et al. 2007).

The acetylene rebreathing procedure was first presented by Grollman (1929). Acetylene diffuses rapidly from the lung into the pulmonary capillaries, and it is highly soluble in blood. In addition, it does not bind with hemoglobin. Therefore, its removal from the lungs is limited by the blood flow through the pulmonary capillaries, and this property is used to estimate Q (Warburton et al. 1998). Although the principle underlying the technique remains the same, the methodology has undergone some modifications (Triebwasser et al. 1977; Smyth et al. 1984). Previous investigators have indicated that the acetylene rebreathing maneuver is difficult to perform during maximal exercise (Warburton et al. 1998; Dibski et al. 2005). Some authors have therefore elected to estimate maximal Q by extrapolating from the submaximal Q to oxygen consumption (VO_2) regression line (Sadaniantz et al. 1996). However, several investigations have demonstrated that it is possible to achieve highly reproducible determinations of Q during maximal exercise (Gledhill et al. 1994; Krip et al. 1997).

Liu et al. (1997) measured Q at rest and during exercise at 25%, 50%, 75% and 90% of $\text{VO}_{2\text{max}}$ by the direct Fick and the acetylene rebreathing method. There were no significant differences in Q measured by each method at rest as well as at each work rate. The difference in Q between each method was greater at a lower Q than at a higher Q. At 90% of $\text{VO}_{2\text{max}}$, the Q measured by acetylene rebreathing was nearly identical to that measured by the Fick method (Liu et al. 1997). This suggests that the acetylene rebreathing method for determining Q is valid not only at rest but also during exercise, especially during high-intensity exercise

Limitations of the method include its insensitivity to anatomical shunt and greater variability in subjects with pulmonary abnormalities. Still, in normal healthy participants these limitations are minimal, and hence the acetylene rebreathing method can provide noninvasive, simple, and valid determinations of Q during increased exercise intensity up to $\text{VO}_{2\text{max}}$ (Warburton et al. 1998).

The aim of present study

Table 1 shows that there is a lack of studies investigating the SV response by increased exercise intensity in female ET subjects. The evidence that male ET individuals are able to increase SV continuously from rest to maximal exercise is compelling (Vanfraechem 1979; Gledhill et al. 1994; Warburton et al. 1999; Zhou et al. 2001; Ramola 2008). Ramola (2008) found that the SV increased progressively with incremental exercise to VO_{2max} in well trained university students (mean VO_{2max} $64 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) using the single breath acetylene method (SB), and exercise levels at rest, 40%, 60%, 80% and 100% of VO_{2max} . A follow up study including ET women could reveal if this SV response also occurs in females. Because cross country skiers are shown to have high VO_{2max} (Saltin and Åstrand 1967; Ingjer 1991; Holmberg et al. 2007), elite female cross country skiers would be relevant subjects studying the SV response with increased intensity in ET women.

Hypothesis

The SV of the heart will increase progressively with exercise intensity to VO_{2max} in elite female cross country skiers.

METHODS

Subjects

13 female cross country skiers participated in this study. Each subject signed consent form approved by the ethical committee and had an examination done by a medical doctor prior to taking part in the study. Table 2 shows the physical characteristics of the participants.

Table 2: Subjects physical characteristics.

N	Age (years)	Height (cm)	Body Mass (kg)	VO_{2max} ($\text{mL}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$)	VO_{2max} ($\text{L}\cdot\text{min}^{-1}$)	VO_{2max} ($\text{mL}\cdot\text{min}^{-1}\cdot\text{kg}^{-0.67}$)
13	22.2 ± 3.0	169 ± 4.8	61.1 ± 6.0	67.1 ± 6.1	4.07 ± 0.22	259.8 ± 17.5

Data are represented as mean \pm standard deviation, VO_{2max} ; Maximal oxygen uptake

Testing apparatus

Treadmill

A Technogym Runrace (Technogym spA, Via Perticary, Italy) treadmill, calibrated for inclination and speed, was used for all physical capacity measurements.

VO_{2max}

The measurements of all respiratory parameters were performed using Cortex Metamax II portable metabolic test system (Cortex Biophysics GmbH, Leipzig, Germany). To analyze the oxygen concentration a Zirconium sensor is used. The volume transducer is connected to a face mask, together with a tube that collects samples of the gas concentration in the mask every 10 seconds. To guarantee that the analyzed gas has a constant humidity, the air from the mask goes through a cylinder with Drierite CaSO_4 , before it enters the capillary sampling tube (Høydal 2003). The gas concentration sensor was calibrated with ambient air and a standardized calibration gas with 16% O_2 , 4% CO_2 and 80% N_2 . The Metamax II has earlier been validated against the classic Douglas bag technique (Larsson et al. 2004). If managed properly, the random error of Metamax II is less than the 1-3% found in biological variation linked to each subject (Medbø et al. 2002).

Heart rate (HR)

HR was measured with a HR monitor (Polar RS400, Polar Electro OY, Kempele, Finland) using a 5-s interval for data storage. The accuracy of HR measurements obtained by Polar Accurex is ± 1 heart beat (Polar Operational Manual 2006).

Cardiac output and stroke volume

For the Q and SV measurements, Sensor Medics Vmax Spectra 229 apparatus (Sensor Medics Corp, California, USA) was used. A flow sensor accurately reads gas temperature as well as molar mass at 8 millisecond intervals and corrects the sample flow and volume instantly. This ensures accurate measurements with any inhaled and exhaled gas also if the room temperature has changed after calibration or during the test itself (Vmax Spectra 229, Operation Manual 2001). This method is called the single breath acetylene method (SB), using a gaseous mixture (Aga, Trondheim, Norway) consisting of 0.3% carbonmonoxide (CO), 0.3% methane (CH₄), 0.3% acetylene (C₂H₂), 21% Oxygen (O₂), and 80% nitrogen (N₂). By measuring the concentrations of CH₄ and C₂H₂, Q can be calculated. A calibration of the flow sensor, with different flow was taken each day after the Vmax was heated for 40 minutes. The calibration was approved if the result was within $\pm 3\%$ of 3 liters. The SB has been validated with the indirect Fick CO₂- rebreathing method and compared with open circuit acetylene uptake. Both techniques were shown to be valid and reliable for measuring Q (Dibski et al. 2005). Repeated measures of Q were made using the SB at rest, 100 W and 200 W. There were no significant differences between repeated measures for this technique at any workload. The standard error of measurements (SEM) decreased with increasing intensity and was 8.5% at rest and 3.2% at 200W. The absolute SEM was similar at all levels of intensity, ranging from 0.47-0.56 (L·min⁻¹). The coefficient of variation was 7.6% at 200W (Dibski et al. 2005). However, the authors concluded that the SB, requiring a constant, slow exhalation rate, made the procedure difficult to perform at the highest exercise intensities (Dibski et al. 2005). Still, most subjects in present study performed the breathing technique at the highest workload without problems. This maybe because the subjects had been familiarized with the breathing technique both at rest and during exercise before the SV test started.

Testing procedure

VO_{2max}

The test was performed with the Metamax II attached to the facemask of the participants. After a 10 min warm up period participants started running at 10.5% of inclination and a speed of 8 km·h⁻¹. Speed was increased by 1 km·h⁻¹ every minute to exhaustion, which occurred in 5-8 min. An approved VO_{2max} was established when VO₂ leveled off in spite of increasing speed, including a respiratory exchange ratio (RER) above 1.05. The highest HR during the last minute determined HR_{max}.

Cardiac output and Stroke volume

Q and SV were measured at least 1 hour after the VO_{2max} test. This period was used to train the subjects in how to perform the breathing technique. The Q measurement procedure started with a complete emptying of the lungs and then maximal inspiration of the gaseous mixture (0.3% CO, 0.3% CH₄, 0.3% C₂H₂, 21% O₂, and 80% N₂), directly followed by one continuous expiration. The same instructions were given to all participants, and all the subjects trained on the breathing technique both during rest and exercise. However, 5 measurements of Q were rejected because the subject did not perform the breathing technique correctly.

The subjects put mouth piece with flow sensor in their mouth, which was connected to the Vmax spectra and went through one testing bout during the rest state. The testing protocol consisted of continuous sequential 4 min work periods. The speed on the treadmill was progressively increased with a constant inclination of 10,5% to elicit steady state conditions at 50%, 70%, 85% and 95% of HR_{max}. When the subjects had maintained their target HR for one minute they were instructed to start the breathing technique. This was to ensure that a steady state had been achieved. HR was measured simultaneously with the breathing technique and was used for the calculation of SV.

Exercise intensities

Four exercise intensities of 40%, 60%, 80%, and 100% of VO_{2max} , were chosen. For practical purposes, we based the relative intensity on % of HR_{max} . American College of Sports Medicine (ACSM) states that 50%, 70%, 85%, and 95% of HR_{max} can be used as equivalent to 40%, 60%, 80%, and 100% of VO_{2max} (Swain et al. 1994).

Statistical analysis

All statistical tests were processed using SPSS 11.0 Software for Windows (SPSS Inc., Chicago, USA). Figure 1 and 2 were made using the GraphPad Prism version 3.00 (Graphpad Software, San Diego, California, USA). To test the assumption of normally distributed data, quantile-quantile (QQ) plots and Shapiro-Wilks test were used. The data material showed normal distribution thus parametric statistics were adopted for the statistical analysis. Further, results are presented as mean and standard deviation (SD). To show variability of sample distribution, standard error of mean is used in figure 1 and 2. One-way ANOVA was used to compare the mean SV and Q at different exercise intensity. Two tailed paired t-tests were used to analyze significant differences between exercise intensities. For all cases statistical significance was set at the level of $P < 0.05$.

RESULTS

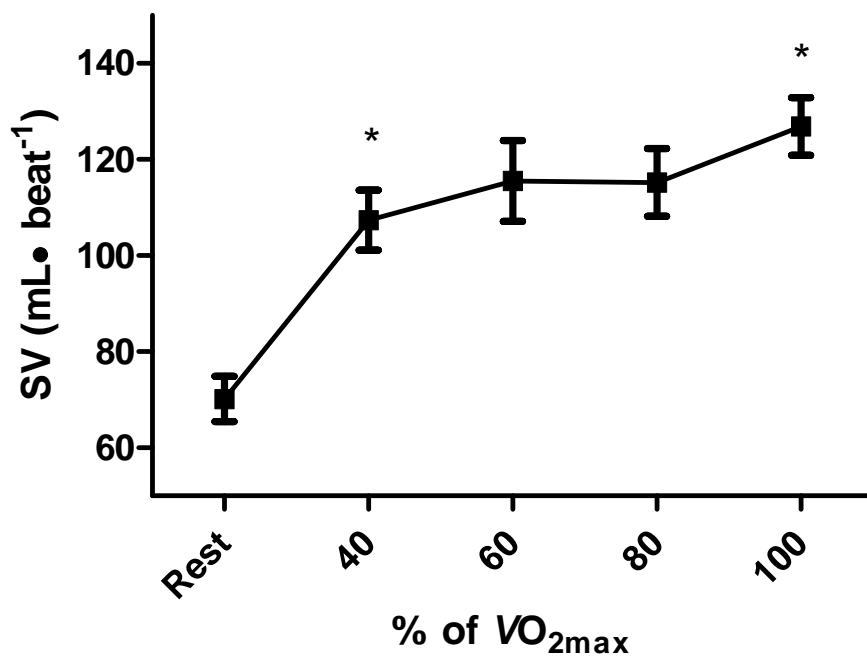
The subject characteristics are presented in table 2. The subject's individual Q and SV measurements are summarized in table 3. Ten of the thirteen subjects achieved their highest SV value at 100% of VO_{2max} . Figure 1 and 2 shows the mean SV and Cardiac output for the 9 participants that performed all the 5 exercise levels.

Table 3: VO_{2max} , HR_{max} , SV and Q data for the individual participant

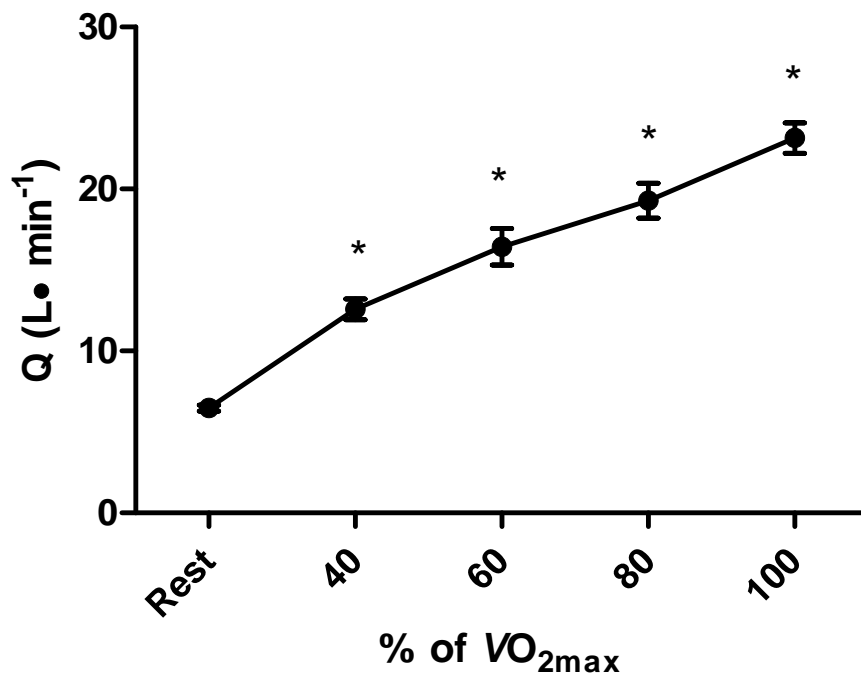
S	VO_{2max} ($mL \cdot min^{-1} \cdot kg^{-1}$)	HR_{max} ($b \cdot min^{-1}$)	SV at % of VO_{2max} ($mL \cdot beat^{-1}$)					Q at % of VO_{2max} ($L \cdot min^{-1}$)				
			Rest	40	60	80	100	Rest	40	60	80	100
1	68.2	186	83.1	-	131.0	138.0	143.0	7.5	-	17.7	22.2	24.7
2	70.9	188	84.2	-	-	118.9	138.3	7.0	-	-	19.6	25.2
3	68.1	193	85.4	115.1	111.8	105.3	119.5	6.8	13.2	15.1	18.0	21.9
4	77.8	195	72.4	112.2	115.3	-	125.6	5.8	13.6	16.1	-	23.7
5	59.4	205	63.8	105.1	117.4	112.4	117.1	6.1	12.2	17.5	19.7	22.1
6	59.2	192	63.6	134.1	131.2	153.5	144.4	5.8	13.8	18.0	24.7	25.9
7	67.5	185	72.0	87.3	103.8	115.2	116.4	6.7	9.2	13.5	18.1	20.7
8	68.0	180	99.4	115.0	134.9	125.1	142.1	6.5	11.8	16.6	18.6	23.9
9	63.5	195	66.2	89.2	83.3	79.2	102.0	6.2	10.9	12.4	13.5	19.0
10	74.2	200	69.3	80.2	76.3	110.5	-	7.0	10.4	11.6	20.1	-
11	72.7	196	56.8	116.5	153.8	135.7	157.5	5.8	14.9	22.8	22.8	28.5
12	65.5	212	55.5	78.5	74.8	105.7	112.1	7.2	11.9	12.9	20.5	22.8
13	57.0	185	68.8	125.4	129.0	104.9	130.8	7.2	15.3	19.2	17.6	23.6
M	67.1	193	72.3	105.3	113.6	117.0	129.1	6.6	12.5	16.1	19.6	23.5
SD	6.1	8.9	12.6	18.8	25.0	19.3	16.3	0.6	1.9	3.2	2.9	2.5

S; Subject, VO_{2max} ; Maximal oxygen consumption, HR_{max} ; Maximal heart rate, SV; Stroke volume, Q; Cardiac Output, M; Mean, SD; Standard deviation.

The repeated measures ANOVA showed statistical significant difference in the SV and the Q measurements at different exercise intensities ($P < 0.05$). Two tailed paired t-tests showed significant increases in SV from rest to 40%, no significant change in SV from 40% to 80% of VO_{2max} , but a significant increase in SV from 80% to VO_{2max} ($P < 0.05$). Q increased significant from rest to 40%, 40% to 60%, 60% to 80% and from 80% to 100% of VO_{2max} ($P < 0.05$).



FIGURE—1 Stroke volume from rest to 100% of VO_{2max} . Mean values and standard error of mean (SEM), for all the subjects that performed all exercise intensities. * SV > than all lower exercise intensities ($p < 0.05$).



FIGURE—2 Cardiac output from rest to maximal exercise. Mean values and SEM for all the subjects that performed all exercise intensities. * Q > than all exercise intensities below ($P < 0.05$).

DISCUSSION

Stroke volume response to increased exercise intensity

The major finding in the present study was that the SV in elite female cross country skiers increased from rest to 40% of VO_{2max} , plateaued from 40% to 80% of VO_{2max} and then increased to VO_{2max} (Fig. 1). This is in line with the results of Ferguson et al. (2001) that showed an increase in SV from 110 bpm to 150-170 bpm, and from 170 bpm to HR_{max} in ET females (mean VO_{2max} 64.3 ml·kg⁻¹·min⁻¹). However, Wiebe et al (1998) investigating exercise cardiac function in young through elderly ET women reported that the SV increased progressively with exercise intensity to VO_{2max} with no plateau, regardless of age. This response is also reported in both ET trained and sedentary male subjects (Gledhill et al. 1994; Krip et al. 1997; Warburton et al. 1999; Zhou et al. 2001; Warburton et al. 2002).

However, the use of exact HR levels in most of these studies makes it difficult to compare the SV response, with present study that used exercise levels predicted by % of VO_{2max} . In present study HR_{max} ranged from 180 bpm to 212 bpm showing the great individual difference in HR_{max} and questions the use of exact HR levels when comparing the SV response with increased exercise intensity between subjects. Still, Ramola (2008) found a progressive increase in the SV of well trained male university students (mean VO_{2max} 62.6 ml·kg⁻¹·min⁻¹) using the same method and measuring levels (40%, 60%, 80% and 100% of VO_{2max}) as the present study. Zhou et al. (2001) reported that the SV of male elite runners increases throughout incremental exercise to maximum using a graded treadmill protocol.

On the other hand, a plateau or a progressive decline in SV with increased intensity from 50-100% of VO_{2max} has been observed in ET females using the acetylene rebreathing method and comparable exercise levels (Ogawa et al. 1992; Proctor et al. 1998). But the subjects in these studies had a much lower VO_{2max} than those in the present study (mean VO_{2max} 45.6 ml·kg⁻¹·min⁻¹ and 52.1 ml·kg⁻¹·min⁻¹). A difference in the SV response between subjects with high and lower VO_{2max} is also reported in male subjects (Crawford et al. 1985; Gledhill et al. 1994; Zhou et al. 2001). However, Ferguson et al. (2001) found an increase in SV from sub maximal levels (110-170bpm) to HR_{max} in moderately active females (mean VO_{2max} 45.6 ml·kg⁻¹·min⁻¹) this is supported by Krip et al. (1997) that reported a progressive increase of SV in untrained male subjects (mean VO_{2max} 41.5 ml·kg⁻¹·min⁻¹).

The conflicting values could be explained by the different methodology and protocols used to assess Q and SV. Most of the studies indicating a rise in the SV with exercise intensity to VO_{2max} used the acetylene rebreathing method (Gledhill et al. 1994; Krip et al. 1997; Wiebe et al. 1998; Warburton et al. 1999; Ferguson et al. 2001; Zhou et al. 2001). Using this method, the measurements are highly dependent upon the subjects' ability to perform the breathing procedure properly. This is more difficult the higher the intensity the measurements are taken at (Dibski et al. 2005).

Interestingly, five of the investigations reporting no plateau in the SV were performed in the same laboratory using a nonconventional supramaximal testing protocol (Rowland 2009). This method included a standard progressive test to volitional exhaustion, but then the subjects were allowed a minute of rest before pedaling again at a supramaximal work load. During this period of exercise, measurement of Q, HR and VO_2 were defined as maximum. It is not clear how much this procedure might influence cardiac dynamics and SV calculation at peak exercise. Hounker et al. (1996) suggested that the increase in SV with progressive exercise in athletes might reflect recruitment of additional muscle groups with improved skeletal muscle pump function, augmented levels of systemic venous return and cardiac filling. Rowland (2009) stated that recruitments of additional muscle groups would be expected during supra- maximal exercise. Further critic against this protocol includes the fact that in three of these studies the final 'maximal' value established the SV pattern as a 'non-plateau'. Also, in the two of the three studies using this protocol that included untrained control subjects, a similar SV response was observed in both trained and untrained subjects (Rowland 2009).

On the other hand, the present study found an increase in SV from 80% of VO_{2max} to VO_{2max} using a continuous graded exercise protocol. This is also reported in other investigations using graded exercise protocols (Zhou et al. 2001; Ramola 2008).

Plateau in SV from 40% to 80% of VO_{2max}

The present study showed a plateau in SV from 40% to 80% of VO_{2max} , before it increased to VO_{2max} . This response is categorized as a plateau with a secondary increase (Vella and Robergs 2005). Chapman et al. 1960 also observed a leveling off in SV at submaximal levels

before exhibiting a secondary increase to VO_{2max} . Ferguson et al. (2001) found a plateau in the SV from HR at 110 bpm to 170 bpm in moderately active females, before it increased to HR_{max} . Martino reported no significant increase in SV between 50-75% of VO_{2max} , but an increase from 75% to 100% of VO_{2max} in untrained men. Krip et al. (1997) found no significant increase in SV from HR at 140 bpm to 180 bpm, investigating ET men.

Interestingly a change point analysis of the SV-slope in elite runners showed a significant change at 89% of HR_{max} (Zhou et al. 2001). This indicates that exercise intensity above 89% of HR_{max} corresponding to approximately 85% of VO_{2max} may be necessary to challenge the heart enough to increase the SV. This is in line with Helgerud et al (2007) that compared the effects of different training intensities on VO_{2max} and SV_{max} in sedentary male subjects. Eight weeks of training revealed no significant increase in SV_{max} in the subjects training on intensities below 85% of HR_{max} , but an increase of 10% was observed in the subjects that performed interval training at intensities 90-95% of HR_{max} . The observed plateau in SV at submaximal levels (40-80% of VO_{2max} , 50-85% of HR_{max}) could explain why the subjects training at intensities below 80% of VO_{2max} didn't increase SV_{max} , but the ones training above 85% of VO_{2max} did. If the work intensity must exceed a certain limit before the heart is challenged enough to increase the SV, this may explain the plateau response observed by Rivera et al. (1989) and Hagberg et al. (1985) who did not measure SV at a higher intensity than 80% of VO_{2max} .

The increase in SV from 40% to 100% of VO_{2max}

With increasing HR, diastolic filling time, as well as systolic ejection time, decreases (Gledhill et al. 1994). The diminished time available for diastolic filling of the left ventricle is thought to lead to a plateau in SV at about 40% of VO_{2max} (Rubal et al. 1986). Still, mean SV in present study showed an increase of 24 ml (23 %) from 40% to 100% of VO_{2max} . This is somewhat lower than reported by Ferguson et al. (2001) that found an increase at 36 ml (44%) from 110 bpm to HR_{max} in ET females. Several of investigations including male ET subjects have reported over 20% increase in the SV from low-mid intensity (30-50% of VO_{2max}) to VO_{2max} (Vanfraechem 1979; Gledhill et al. 1994; Krip et al. 1997; Warburton et al. 1999; Ferguson et al. 2001; Zhou et al. 2001; Warburton et al. 2002; Ramola 2008).

Current research suggests enhanced diastolic filling with a reliance on a Frank-Starling mechanism to augment SV as work intensity rises, to be the main mechanism behind the increase in SV observed in male ET subjects (Wolfe et al. 1978; Gledhill et al. 1994; Krip et al. 1997; Ferguson et al. 2001; Vinereanu et al. 2002). Ferguson et al. (2001) concluded that female subjects have a similar exercise cardiac function as men and the same mechanism are responsible for the observed increase in SV to VO_{2max} .

However, a 20 mL (29%) increase in SV from 110 bpm to HR_{max} was found in moderately active females, and an increase of 15 mL (13 %) from 120 bpm to HR_{max} was reported in untrained men (Krip et al. 1997; Ferguson et al. 2001). This indicates that cardiac adaptations as a consequence of endurance training are not necessary to obtain an increase in SV from submaximal levels to VO_{2max} .

SV_{max}

The mean SV_{max} in present study was $129 \text{ ml}\cdot\text{beat}^{-1}$ and is higher than reported by others investigating ET females at the same age (Ogawa et al. 1992; Ferguson et al. 2001). However, the women in these studies had lower VO_{2max} ($\text{l}\cdot\text{min}^{-1}$) than present study. This is in line with Basset and Howley (2000), who stated that the range of VO_{2max} ($\text{l}\cdot\text{min}^{-1}$) observed in sedentary and trained men and women at the same age is due principally to variation in SV_{max} , given that considerably less variation exists in maximal HR and systemic oxygen extraction.

SV_{max} in present study is lower than reported for male ET subjects with approximately similar VO_{2max} ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-0.67}$) (Ogawa et al. 1992; Krip et al. 1997; Martino et al. 2002; Ramola 2008). Ogawa et al. (1992) reported that the SV of women was lower at all workloads compared with men, even after normalization to body weight. After normalization of SV to fat free mass, the gender difference was eliminated in sedentary subjects, but only reduced in the ET subjects. The authors concluded that the gender difference in the SV of the ET subjects was due to a greater percentage of body fat in women (Ogawa et al. 1992).

Cardiac output

As expected, Q increased progressively from rest to maximal exercise. Mean value for Q_{\max} in present study was $23.5 \text{ L}\cdot\text{min}^{-1}$. This is about the same reported by Ferguson et al. (2001) ($23.3 \text{ L}\cdot\text{min}^{-1}$) including ET females, and suggesting that the acetylene rebreathing technique can be used with confidence to assess Q throughout incremental exercise, including maximal work rate. However, Ferguson et al. (2001) used two sequential Q measurements which were conducted 45s apart to complete total washout of acetylene. Mean Q_{\max} in present was lower than observed in male endurance athletes (Gledhill et al. 1994; Krip et al. 1997; Zhou et al. 2001), but comparable with male ET subjects at the same $VO_{2\max}$ level ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-0.67}$) (Vanfraechem 1979; Ogawa et al. 1992; Martino et al. 2002; Ramola 2008).

$VO_{2\max}$

Mean $VO_{2\max}$ for the thirteen elite cross country skiers in present study were $67.1 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ($4.1 \text{ L}\cdot\text{min}^{-1}$, $260 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-0.67}$). This represents the highest $VO_{2\max}$ value reported in female subjects investigating the SV response (table 1). This is in line with current research suggesting cross country skiers to be among the endurance athletes with the highest $VO_{2\max}$ (Saltin and Åstrand 1967; Ingjer 1991; Holmberg et al. 2007). Saltin et al. (1967) reported mean $VO_{2\max}$ at $63.6 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ ($3.75 \text{ L}\cdot\text{min}^{-1}$) in female cross country skiers and concluded that this was higher than the $VO_{2\max}$ values observed in other endurance sports as orienteering, running and swimming. It has also been reported that elite cross country skiers reach higher $VO_{2\max}$ values while combining arm and leg exercise compared to running, although the difference is quite small (Holmberg et al. 2007). Ingjer (1991) reported the mean $VO_{2\max}$ in both world class and medium class elite female skiers to be approximately $70 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. However, using scaled values the elite women showed significantly higher $VO_{2\max}$, $274 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-0.67}$ compared to $264 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-0.67}$ in the medium elite group. The author concluded that $VO_{2\max}$ expressed as $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-0.67}$ reflects differences in performance capability among elite skiers better than the unit $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (Ingjer 1991). Mean $VO_{2\max}$ in present study ($260 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-0.67}$) is at the same level as the medium class elite in the study by Ingjer (1991) ($264 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-0.67}$).

CONCLUSIONS

The SV in the present elite female cross country skiers increased from rest to 40% of VO_{2max} , plateaued from 40-80 % of VO_{2max} and then increased from 80-100% of VO_{2max} . The hypothesis of a continuous increase in SV when training intensities increased from 40 to 100% of VO_{2max} was thus rejected.

Practical application of the study

When endurance athletes try to select the most optimal training program for a specific sport, it is very important to know how different training intensities influence adaptations in physiological parameters.

At maximal exercise, the majority of evidence points to a VO_{2max} that is limited by oxygen supply, and Q seems to be the major factor determining oxygen delivery (Wagner 1996). It is estimated that 70–85% of the limitation in VO_{2max} is linked to maximal cardiac output (Cerretelli and Di Prampero 1987). Since HR does not change much with training, the main potential to increase Q is through increasing the SV. SV of the heart is known as the most important limitation of the VO_{2max} (Bassett and Howley 2000).

The present study showed a significant increase in the SV, from 80% to 100% of VO_{2max} . This indicates that an exercise intensity corresponding to 100% of VO_{2max} approximately 95% of HR_{max} is necessary to attain the highest SV. No significant increase in SV was observed from 40% to 80% of VO_{2max} . This corresponds to 50-85 % of HR_{max} suggesting that exercise intensity below 85% of VO_{2max} will not stimulate SV adaptations optimally. This is also in line with conclusions in training studies where low intensity- and high aerobic intensity exercise are compared (Helgerud et al. 2007).

References

- Ahmad, M. and J. P. Dubiel (1990). "Left ventricular response to exercise in regular runners and controls. A radionuclide evaluation." Clin Nucl Med **15**(9): 630-635.
- Bassett, D. R., Jr. and E. T. Howley (2000). "Limiting factors for maximum oxygen uptake and determinants of endurance performance." Med Sci Sports Exerc **32**(1): 70-84.
- Bevegard, S., A. Holmgren and B. Jonsson (1963). "Circulatory studies in well trained athletes at rest and during heavy exercise. With special reference to stroke volume and the influence of body position." Acta Physiol Scand **57**: 26-50.
- Ceretelli, P. and P. E. Di Prampero (1987). Gas exchange in exercise. Bethesda, American Physiological Society, .
- Crawford, M. H., M. A. Petru and C. Rabinowitz (1985). "Effect of isotonic exercise training on left ventricular volume during upright exercise." Circulation **72**(6): 1237-1243.
- Dibski, D. W., D. J. Smith, R. Jensen, S. R. Norris and G. T. Ford (2005). "Comparison and reliability of two non-invasive acetylene uptake techniques for the measurement of cardiac output." Eur J Appl Physiol **94**(5-6): 670-680.
- Ekblom, B. and L. Hermansen (1968). "Cardiac output in athletes." J Appl Physiol **25**(5): 619-625.
- Ferguson, S., N. Gledhill, V. K. Jamnik, C. Wiebe and N. Payne (2001). "Cardiac performance in endurance-trained and moderately active young women." Med Sci Sports Exerc **33**(7): 1114-1119.
- Finkelhor, R. S., L. J. Hanak and R. C. Bahler (1986). "Left ventricular filling in endurance-trained subjects." J Am Coll Cardiol **8**(2): 289-293.
- Gledhill, N., D. Cox and R. Jamnik (1994). "Endurance athletes' stroke volume does not plateau: major advantage is diastolic function." Med Sci Sports Exerc **26**(9): 1116-1121.
- Grimby, G., N. J. Nilsson and B. Saltin (1966). "Cardiac output during submaximal and maximal exercise in active middle-aged athletes." J Appl Physiol **21**(4): 1150-1156.
- Grollman, A. (1929). "VARIATIONS IN THE CARDIAC OUTPUT OF MAN: V. The Cardiac Output of Man During the Malaise and Pyrexia Following the Injection of Typhoid Vaccine." J Clin Invest **8**(1): 25-32.

- Hagberg, J. M., W. K. Allen, D. R. Seals, B. F. Hurley, A. A. Ehsani and J. O. Holloszy (1985). "A hemodynamic comparison of young and older endurance athletes during exercise." J Appl Physiol **58**(6): 2041-2046.
- Helgerud, J., K. Hoydal, E. Wang, T. Karlsen, P. Berg, M. Bjerkaas, T. Simonsen, C. Helgesen, N. Hjorth, R. Bach and J. Hoff (2007). "Aerobic high-intensity intervals improve VO2max more than moderate training." Med Sci Sports Exerc **39**(4): 665-671.
- Higginbotham, M. B., K. G. Morris, R. S. Williams, P. A. McHale, R. E. Coleman and F. R. Cobb (1986). "Regulation of stroke volume during submaximal and maximal upright exercise in normal man." Circ Res **58**(2): 281-291.
- Holmberg, H. C., H. Rosdahl and J. Svedenhag (2007). "Lung function, arterial saturation and oxygen uptake in elite cross country skiers: influence of exercise mode." Scand J Med Sci Sports **17**(4): 437-444.
- Hoogsteen, J., A. Hoogeveen, H. Schaffers, P. F. Wijn and E. E. van der Wall (2003). "Left atrial and ventricular dimensions in highly trained cyclists." Int J Cardiovasc Imaging **19**(3): 211-217.
- Hopper, M. K., A. R. Coggan and E. F. Coyle (1988). "Exercise stroke volume relative to plasma-volume expansion." J Appl Physiol **64**(1): 404-408.
- Hsia, C. C., L. F. Herazo, M. Ramanathan and R. L. Johnson, Jr. (1995). "Cardiac output during exercise measured by acetylene rebreathing, thermodilution, and Fick techniques." J Appl Physiol **78**(4): 1612-1616.
- Huonker, M., D. Konig and J. Keul (1996). "Assessment of left ventricular dimensions and functions in athletes and sedentary subjects at rest and during exercise using echocardiography, Doppler sonography and radionuclide ventriculography." Int J Sports Med **17 Suppl 3**: S173-179.
- Høydal, M. A. (2003). "The correlation between derite CaSO4 and Nafion membrane tube when measuring oxygen consumption using the Cortex Metamax II portable ergospirometry system. ." Unpub. Pilot paper. Faculty of Medicine, NTNU, .
- Ingjer, F. (1991). "Maximal oxygen uptake as a predictor of performance ability in woman and man elite cross-country skiers. ." Scand Med Sport Exerc **1**(1): 5.
- Jarvis, S. S., B. D. Levine, G. K. Prisk, B. E. Shykoff, A. R. Elliott, E. Rosow, C. G. Blomqvist and J. A. Pawelczyk (2007). "Simultaneous determination of the accuracy and precision of closed-circuit cardiac output rebreathing techniques." J Appl Physiol **103**(3): 867-874.

- Kanstrup, I. L. and B. Ekblom (1982). "Acute hypervolemia, cardiac performance, and aerobic power during exercise." J Appl Physiol **52**(5): 1186-1191.
- Krip, B., N. Gledhill, V. Jamnik and D. Warburton (1997). "Effect of alterations in blood volume on cardiac function during maximal exercise." Med Sci Sports Exerc **29**(11): 1469-1476.
- Larsson, P. U., K. M. Wadell, E. J. Jakobsson, L. U. Burlin and K. B. Henriksson-Larsen (2004). "Validation of the MetaMax II portable metabolic measurement system." Int J Sports Med **25**(2): 115-123.
- Laszlo, G. (2004). "Respiratory measurements of cardiac output: from elegant idea to useful test." J Appl Physiol **96**(2): 428-437.
- Levine, B. D., L. D. Lane, J. C. Buckey, D. B. Friedman and C. G. Blomqvist (1991). "Left ventricular pressure-volume and Frank-Starling relations in endurance athletes. Implications for orthostatic tolerance and exercise performance." Circulation **84**(3): 1016-1023.
- Levy, W. C., M. D. Cerqueira, I. B. Abrass, R. S. Schwartz and J. R. Stratton (1993). "Endurance exercise training augments diastolic filling at rest and during exercise in healthy young and older men." Circulation **88**(1): 116-126.
- Liu, Y., E. Menold, A. Dullenkopf, S. Reissnecker, W. Lormes, M. Lehmann and J. M. Steinacker (1997). "Validation of the acetylene rebreathing method for measurement of cardiac output at rest and during high-intensity exercise." Clin Physiol **17**(2): 171-182.
- Martino, M., N. Gledhill and V. Jamnik (2002). "High VO₂max with no history of training is primarily due to high blood volume." Med Sci Sports Exerc **34**(6): 966-971.
- McArdle, W. D., F. I. Katch and V. L. Katch (2006). Exercise Physiology Energy, Nutrition & Human Performance, Lippincott Williams & Wilkins.
- McLaren, P. F., Y. Nurhayati and S. H. Boutcher (1997). "Stroke volume response to cycle ergometry in trained and untrained older men." Eur J Appl Physiol Occup Physiol **75**(6): 537-542.
- Medbø, J. I., A. Mamen, B. Welde, E. von Heimburg and R. Stokke (2002). "Examination of the Metamax I and II oxygen analysers during exercise studies in the laboratory." Scand J Clin Lab Invest **62**(8): 585-598.

- Mier, C. M., M. A. Domenick, N. S. Turner and J. H. Wilmore (1996). "Changes in stroke volume and maximal aerobic capacity with increased blood volume in men women." J Appl Physiol **80**(4): 1180-1186.
- Ogawa, T., R. J. Spina, W. H. Martin, 3rd, W. M. Kohrt, K. B. Schechtman, J. O. Holloszy and A. A. Ehsani (1992). "Effects of aging, sex, and physical training on cardiovascular responses to exercise." Circulation **86**(2): 494-503.
- Patel, C., V. Laboy, B. Venus, M. Mathru and D. Wier (1986). "Acute complications of pulmonary artery catheter insertion in critically ill patients." Crit Care Med **14**(3): 195-197.
- Polar Electro, RS400 Operational Manual (2006). Kempele, Finland.
- Proctor, D. N., K. C. Beck, P. H. Shen, T. J. Eickhoff, J. R. Halliwill and M. J. Joyner (1998). "Influence of age and gender on cardiac output-VO₂ relationships during submaximal cycle ergometry." J Appl Physiol **84**(2): 599-605.
- Ramola, K. (2008). Effect of the incremental exercise intensity on the stroke volume of well trained subjects. Department of Circulation and Medical Imaging Faculty of Medicine Trondheim, Norwegian University of Science and Technology. Master.
- Rerych, S. K., P. M. Scholz, D. C. Sabiston, Jr. and R. H. Jones (1980). "Effects of exercise training on left ventricular function in normal subjects: a longitudinal study by radionuclide angiography." Am J Cardiol **45**(2): 244-252.
- Rivera, A. M., A. E. Pels, 3rd, S. P. Sady, M. A. Sady, E. M. Cullinane and P. D. Thompson (1989). "Physiological factors associated with the lower maximal oxygen consumption of master runners." J Appl Physiol **66**(2): 949-954.
- Rowland, T. (2009). "Endurance athletes' stroke volume response to progressive exercise: a critical review." Sports Med **39**(8): 687-695.
- Rubal, B. J., J. M. Moody, S. Damore, S. R. Bunker and N. M. Diaz (1986). "Left ventricular performance of the athletic heart during upright exercise: a heart rate-controlled study." Med Sci Sports Exerc **18**(1): 134-140.
- Sadaniantz, A., S. Yurgalevitch, J. M. Zmuda and P. D. Thompson (1996). "One year of exercise training does not alter resting left ventricular systolic or diastolic function." Med Sci Sports Exerc **28**(11): 1345-1350.

- Saltin, B. and P. O. Åstrand (1967). "Maximal oxygen uptake in athletes." J Appl Physiol **23**(3): 353-358.
- Simmons, R. and R. J. Shephard (1971). "Measurements of cardiac output in maximum exercise. Application of an acetylene rebreathing method to arm and leg exercise." Int Z Angew Physiol **29**(2): 159-172.
- Smyth, R. J., N. Gledhill, A. B. Froese and V. K. Jamnik (1984). "Validation of noninvasive maximal cardiac output measurement." Med Sci Sports Exerc **16**(5): 512-515.
- Spina, R. J., T. Ogawa, W. H. Martin, 3rd, A. R. Coggan, J. O. Holloszy and A. A. Ehsani (1992). "Exercise training prevents decline in stroke volume during exercise in young healthy subjects." J Appl Physiol **72**(6): 2458-2462.
- Stevenson, E. T., K. P. Davy and D. R. Seals (1994). "Maximal aerobic capacity and total blood volume in highly trained middle-aged and older female endurance athletes." J Appl Physiol **77**(4): 1691-1696.
- Sullivan, M. J., F. R. Cobb and M. B. Higginbotham (1991). "Stroke volume increases by similar mechanisms during upright exercise in normal men and women." Am J Cardiol **67**(16): 1405-1412.
- Swain, D. P., K. S. Abernathy, C. S. Smith, S. J. Lee and S. A. Bunn (1994). "Target heart rates for the development of cardiorespiratory fitness." Med Sci Sports Exerc **26**(1): 112-116.
- Triebwasser, J. H., R. L. Johnson, R. P. Burpo, J. C. Campbell, W. C. Reardon and C. G. Blomqvist (1977). "Noninvasive determination of cardiac output by a modified acetylene rebreathing procedure utilizing mass spectrometer measurements." Aviat Space Environ Med **48**(3): 203-209.
- Vanfraechem, J. H. (1979). "Stroke volume and systolic time interval adjustments during bicycle exercise." J Appl Physiol **46**(3): 588-592.
- Vella, C. A. and R. A. Robergs (2005). "A review of the stroke volume response to upright exercise in healthy subjects." Br J Sports Med **39**(4): 190-195.
- Vmax Spectra 229 Operation Manual (2001), Sensormedics Inc., USA.

- Vinereanu, D., N. Florescu, N. Sculthorpe, A. C. Tweddel, M. R. Stephens and A. G. Fraser (2002). "Left ventricular long-axis diastolic function is augmented in the hearts of endurance-trained compared with strength-trained athletes." Clin Sci (Lond) **103**(3): 249-257.
- Wagner, P. D. (1996). "A theoretical analysis of factors determining VO₂ MAX at sea level and altitude." Respir Physiol **106**(3): 329-343.
- Warburton, D. E., N. Gledhill and V. K. Jamnik (1998). "Reproducibility of the acetylene rebreath technique for determining cardiac output." Med Sci Sports Exerc **30**(6): 952-957.
- Warburton, D. E., N. Gledhill, V. K. Jamnik, B. Krip and N. Card (1999). "Induced hypervolemia, cardiac function, VO₂max, and performance of elite cyclists." Med Sci Sports Exerc **31**(6): 800-808.
- Warburton, D. E., M. J. Haykowsky, H. A. Quinney, D. Blackmore, K. K. Teo and D. P. Humen (2002). "Myocardial response to incremental exercise in endurance-trained athletes: influence of heart rate, contractility and the Frank-Starling effect." Exp Physiol **87**(5): 613-622.
- Wiebe, C. G., N. Gledhill, D. E. Warburton, V. K. Jamnik and S. Ferguson (1998). "Exercise cardiac function in endurance-trained males versus females." Clin J Sport Med **8**(4): 272-279.
- Wolfe, L. A., D. A. Cunningham, G. M. Davis and H. Rosenfeld (1978). "Relationship between maximal oxygen uptake and left ventricular function in exercise." J Appl Physiol **44**(1): 44-49.
- Zhou, B., R. K. Conlee, R. Jensen, G. W. Fellingham, J. D. George and A. G. Fisher (2001). "Stroke volume does not plateau during graded exercise in elite male distance runners." Med Sci Sports Exerc **33**(11): 1849-1854.
- Åstrand, P. O., T. E. Cuddy, B. Saltin and J. Stenberg (1964). "Cardiac Output during Submaximal and Maximal Work." J Appl Physiol **19**: 268-274.