Chapter

Mechanical Limits of Cardiac Output at Maximal Aerobic Exercise

Sheldon Magder

Abstract

This chapter uses an analytic approach to the factors limiting maximal aerobic exercise. A person's maximal aerobic work is determined by their maximal oxygen consumption (VO_2max). Cardiac output is the dominant determinant of VO_2 and thus the primary determinant of population differences in VO_2max. Furthermore, cardiac output is the product of heart rate and stroke volume and maximum heart rate is determined solely by a person's age. Thus, maximum stroke volume is the major factor for physiological differences in aerobic performance. Stroke output must be matched by stroke volume return, which is determined by the mechanical properties of the systemic circulation. These are primarily the compliances of each vascular region and the resistances between them. I first discuss the physiological principles controlling cardiac output and venous return. Emphasis is placed on the importance of the distribution of blood flow between the parallel compliances of muscle and splanchnic beds as described by August Krogh in 1912. I then present observations from a computational modeling study on the mechanical factors that must change to reach known maximum cardiac outputs during aerobic exercise. A key element that comes out of the analysis is the role of the muscle pump in achieving high cardiac outputs.

Keywords: aerobic limit, oxygen consumption, stressed volume, venous return, cardiac output, stroke volume, heart rate, time constants

1. Introduction

Sustainable work at high levels of energy consumption requires oxygen (O_2) based metabolism. Maximum O_2 consumption (VO_2) thus determines a person's maximal aerobic power [1]. A young active healthy male of standard size can increase VO_2 from a resting value of around 0.25 L/min to between 3.00 and 3.5 L/min, a 12–14 fold increase [1, 2]. In elite athletes, values greater than 6.0 L/min have been measured [3]. The physiological basis of these numbers can be understood by considering the Fick principle, which is essentially a statement of the conservation of mass [1, 4]. VO_2 is the product of how much volume per minute/min (L/min) is delivered to tissues, in other words, cardiac output, and how much O_2 is extracted from each volume unit of blood [1, 2].

$$\dot{V}O_2 = Q\,x\left[Hb\right]x1.36\left(Sat_aO_2 - Sat_vO_2\right) \quad (1)$$

Q is cardiac output (L/min), [Hb] is hemoglobin concentration (in g/L), 1.36 is the constant for the amount of O_2 (ml) per g of Hb, Sat_aO_2 is the arterial O_2 saturation (as a decimal) and Sat_vO_2 is the venous O_2 saturation (as a decimal). Thus, the limit of aerobic function is based on the maximum extraction of O_2 from the blood and the maximum cardiac output.

The capacity of arterial blood to carry O_2 is determined by the concentration of hemoglobin ([Hb]) and the amount of O_2 that each gram of Hb can bind [5]. The constant for binding of O_2 to Hb with no other substances present is 1.39 ml O_2 per gram of Hb, but normally other molecules in blood, such as methemoglobin and carboxyhemoglobin, take up some of the binding sites. Thus, constants of 1.34–1.39 are used in the literature to account for these factors. The actual content of O_2 in blood is dependent upon [Hb] and the saturation of Hb molecules with O_2; the saturation is in-turn is dependent upon the partial pressure of O_2 in blood (PO_2 in mmHg). [Hb] concentration thus sets the upper limit of how much O_2 is present to be extracted from the blood. As an example, with a [Hb] of 145 g/L, a saturation of 98%, and capacity of Hb to carry O_2 of 1.36 ml O_2/g Hb, the arterial O_2 content would be 197.1 ml/L. The saturation of arterial blood usually is slightly less than 100% because of some shunting of blood across the lungs and venous blood returning to the left ventricle from the coronary circulation. [Hb] is similar in a standard male and endurance athlete (unless there has been some kind of unfair manipulation of [Hb]!) so that this factor does not play a large role in differences in maximum VO_2. During exercise [Hb] increases slightly because of a loss of plasma and hemoconcentration [6].

The O_2 content of blood returning to the right heart gives the overall extraction of O_2 by all tissues. This is called mixed venous O_2 content (M_vO_2). At rest, about 25% of the arterial blood O_2 content is extracted, which gives a M_vO_2 of around 150 ml/L in both a standard male and elite athlete [6]. During peak aerobic exercise, the greatest proportion of the blood goes to the working muscle, which is capable of extracting almost all the delivered O_2 it receives at peak performance. Under resting conditions about 60% of blood flow goes to the muscle vasculature and 40%, or about 2 L/min, goes to the non-muscle vasculature [7, 8]. At peak exercise, the amount going to non-working muscle remains largely unchanged, or decreases by a small amount, so that greater than 90% of blood flow goes to the working muscle [7], which at peak performance can extract almost all the O_2 it receives. The percent of blood flow going to non-working tissues sets a lower limit of O_2 extraction [9]. The maximal amount of O_2 extracted is similar in standard young healthy males and endurance athletes, although extraction can be slightly greater in endurance athletes. This is likely because they have larger amount of muscle mass per total body mass, and thus a higher fraction of blood flow can go to the working muscle, which results in greater total extraction. A greater capacity to endure discomfort may also play a role. A typical M_vO_2 at peak performance is in the range of 22 ml/L in the standard male and 18 ml/L in elite endurance athletes, which is less than a 1% difference in the total amount extracted [10]. Thus, differences in O_2 extraction between standard and elite athletes contribute little to differences in their maximum VO_2 unless the arterial O_2 carrying capacity is significantly increased, although this potentially could limit extraction by increasing blood viscosity and reducing blood flow to tissues.

Based on the Fick equation, the other determinant of maximum VO_2 is cardiac output. In a typical young male, cardiac output can increase from a resting value of around 5 L/min to 20–25 L/min, a 4–5 fold increase [1, 2]. In elite athletes maximal cardiac output can be in the range of 30 L/min to even over 40 L/min in some high performing cyclist and cross-country skiers [11]. The athletes thus can have a 6–7 fold increase in cardiac output from resting levels and this increase in cardiac

output is the major factor explaining their higher aerobic capacity [4]. If [Hb] is normal there is a tight linear relationship between cardiac output and VO_2 that is independent of body size, fitness, or age [2, 4]. The slope of this relationship is the same in women and men but the relationship is shifted downward in women because of they generally have lower [Hb] [2].

Cardiac output is the product of beats per minute, that is, heart rate, and stroke volume. Maximum heart rate at peak aerobic performance is solely determined by age and not by differences in fitness, body size, heart size, or sex; the rise in heart rate is dependent upon the percent of the maximal capacity of the muscles being used [2]. This means that the primary difference in aerobic power of the standard male and elite aerobic athletes is the maximum possible stroke volume for that person [1, 3]. Furthermore, stroke volume is dependent upon heart size, which for healthy hearts is related to lean body size as determined by the person's genetic make-up [12]. There is little change in stroke volume capacity with training [10], although increases in maximum stroke volume often are observed in studies with training [10, 13]. These observed increases in stroke volume are likely related to reductions in submaximal heart rate, which occur due to alterations in neuro-humeral mechanisms with training [9]. A lower heart rate at a given VO_2 requires that there be a larger stroke volume for the same venous return and cardiac output so that the relationship of cardiac output to VO_2 is maintained, but this does not mean that there was an intrinsic change in heart structure.

2. Basic principles of the determinants of blood flow in the circulation

It often is thought that blood flow around the circuit is dependent on the arterial pressure regenerated by the heart [14]. This view is of presented as an electrical model with the arterial pressure being the equivalent of a fixed voltage from a source. In this construct, vascular volume, which the electrons in the circuit, is not a fixed value, but can increase or fall based on current for the fixed pressure drop. In contrast, Arthur Guyton [15], and for that matter, Ernest Starling [16], used a hydraulic approach in which the elastic energy, that is pressure, produced by a fixed volume in the circuit determines the return of blood to the heart. The action of the heart in this approach is to pump the returning blood back to the circuit [17]. In the Guyton approach, blood flow around the circuit is determined by two functions: cardiac function and a function that describes the return of blood to the heart from a large venous compliant region [15]. These are discussed next.

2.1 Cardiac function

The basis of cardiac function is the Frank-Starling law, which says that the greater the initial cardiac muscle length the greater the force produced by the heart up to a limit [16]. The determinants of cardiac output are heart rate and stroke volume, and stroke volume is determined by the preload, afterload and contractility. Cardiac function is plotted with right atrial pressure (Pra) at the end-of diastole. This determines right ventricular end-diastolic muscle length, and the preload, on the x-axis, and cardiac output on the y-axis (**Figure 1**) [18]. This relationship assumes a constant heart rate, afterload and contractility. An increase in cardiac function is produced by an increase in heart rate, increase in contractility, or a decrease in afterload and is indicated by upward shift of the curve (**Figure 1**). The opposites cause a decrease in cardiac function and a

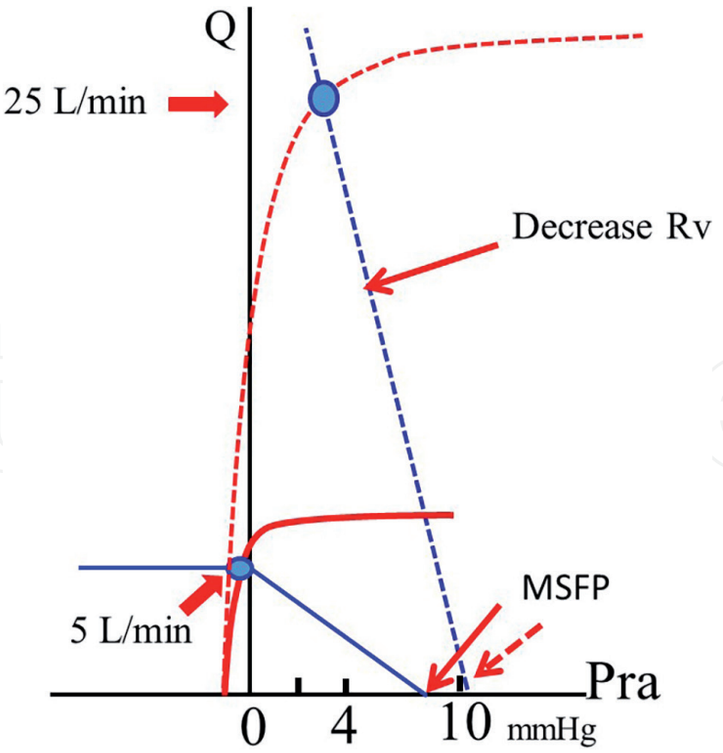

Figure 1.
Schematic plots of venous return and cardiac function curves at rest and maximal aerobic exercise. The resting state is shown with solid lines and exercise state with dashed lines. The change in cardiac output was from 5 to 25 L/min. The x-axis is right atrial pressure (Pra) in mmHg and the y-axis is blood flow in L/min. The curved red lines are cardiac function curves and the blue lines are venous return curves. The slope of the venous return curve is −1/resistance to venous return (Rv). During exercise there is a marked increase in the cardiac function curve due to primarily to the rise in heart rate and to a lesser extent, stroke volume. This is matched by a marked decrease in Rv and a small increase in MSFP due a decrease in vascular capacitance.

downward shift of the curve. Importantly, the cardiac function curve has a sharp plateau [19], and when reached, further increases in preload, that is Pra, do not increase cardiac output.

2.2 Venous return function

The typical total blood volume of a 70 kg male is approximately 5.5 L. When there is no flow in the circulation the contained volume still stretches vascular walls and creates a pressure of 7–10 mmHg; this is called mean circulatory filling pressure (MCFP) [15, 20]. About 70% of vascular volume resides in small veins and venules. The compliance of the walls of these vessels, that is change in volume per change in pressure, is 30–40 times greater than that of arterial and capillary vessels and seven times the compliance of the pulmonary vessels [21]; because systemic veins dominate the volume of the circulation, they are the major determinant of MCFP [22]. Under flow conditions, volume redistributes throughout the vasculature so that there can be some change in volume and pressure in the veins and venules. Since the pressure in veins and venules is the upstream pressure determining blood return to the heart, it is given a separate name, mean systemic filling pressure (MSFP). When there is no flow, MSFP and MCFP are equal as is Pra.

Another important concept is vascular capacitance [23, 24]. Some of the total vascular volume just rounds out vessels, but this volume does not stretch vessel walls. This volume is thus "unstressed" in that it does not produce a pressure. Only the volume above unstressed volume stretches vessels walls and accordingly is called stressed volume. Under resting conditions about 70% of blood volume is unstressed and 30%, or about 1.3–1.4 L, is stressed [25]. Only this stressed volume produces

the elastic force that drives venous blood back to the heart. However, activation of sympathetic activity can result in constriction of veins and venules and thereby convert unstressed into stressed volume [24, 26–28]. By this means, unstressed volume acts as a vascular reserve, and stressed volume can be increased by 6–10 ml/kg, and sometimes more. This is the equivalent to a vascular infusion of fluid and can greatly increase MSFP almost instantly.

Venous blood returns to the right heart through the resistance downstream from the venous compliant regions [15]. Although small, and only produces a pressure drop only of 4–8 mmHg, this resistance it is a major determinant of the return of blood to the heart because it controls the emptying of the large upstream venous reservoir.

The final determinant of venous return is Pra. This is the downstream pressure for venous drainage. In this context, it can be considered that the primary role of the heart in the control of cardiac output is to keep Pra low so as to allow venous return [18]. In this sense, the right ventricle has primarily a "permissive function" in that it "allows" venous blood to return. Importantly, the best that the heart can do is lower Pra to zero, that is, atmospheric pressure. Below this value the pressure inside the floppy great veins is less than the surrounding pressure and collapse, thereby creating flow limitation or what is called a vascular waterfall. When this happens, lowering Pra further does not increase venous return and accordingly, cardiac output [29].

Venous return was plotted by Arthur Guyton with flow on the y-axis and Pra on the x-axis (**Figure 1**) [15]. The x-intercept is MSFP and the slope of the line is the negative inverse of the resistance to venous return (−1/Rv). The venous return curve has the same axes as the cardiac function curve. Thus cardiac function and return function can be plotted on the same graph and this plot can be used to mathematically solve the interaction of these two functions [15].

2.3 Interaction of the return function and cardiac function

Actual cardiac output is determined by the intersection of the cardiac function and return function (**Figure 1**) [15]. An isolated increase in cardiac function produces an increase in cardiac output and a decrease in Pra. An isolated increase in the return function produces an increase in cardiac output with a rise in Pra [18]. A study in normal young males showed that at the onset of pedaling on an upright stationary cycle, Pra immediately increased from –2 to ~4 mmHg [30] and then changed little all the way to maximum effort [31]. This indicates that after an initial moderate increase in preload because of volume being squeezed out the working muscle, increases in cardiac and return functions are perfectly matched. Interestingly, in a group of patients with denervated transplanted hearts, although it took a longer time for equilibration to occur, as exercise continued they too had little change in Pra with increasing cardiac outputs. The slope of the rise in their cardiac output with the rise in VO_2 also was the same range as normal subjects [31–33].

2.4 Two compartment model

So far in this discussion, I have applied the Guyton model of the circulation which considers that there is only one large venous compliant region [20]. In 1912 August Krogh [34] observed that if a closed circuit has two regions with different compliances in parallel, changes in the fractional distribution of flow between the two regions produced by changes in their inflow resistances, alters the rate of flow around the system (**Figure 2**). This is because when more volume goes to the less compliant region, the pressure rises in this region, which then increases the rate of

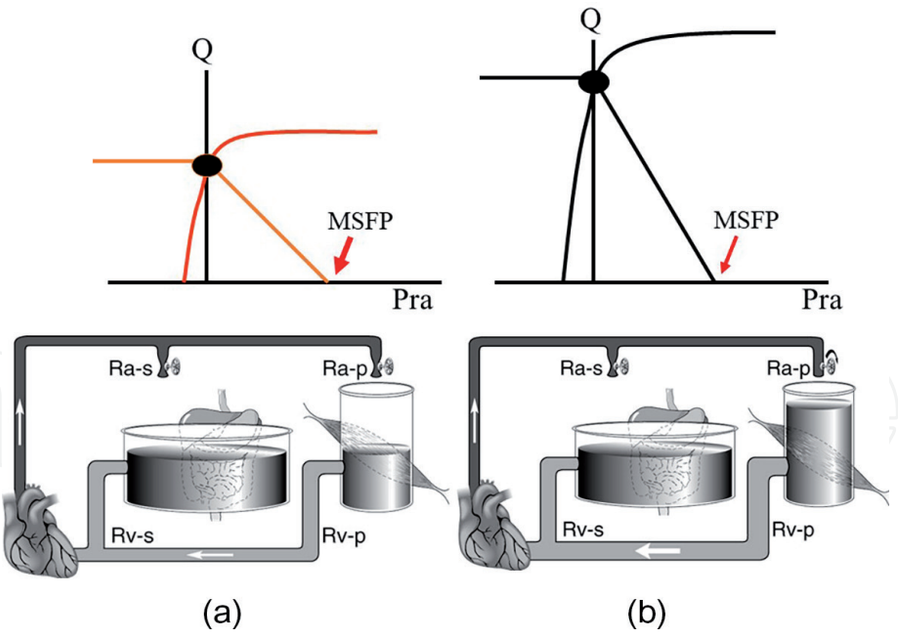

Figure 2.
The two compartment model of the circulation—Krogh model. In this model there are two parallel venous compartments. One, the equivalent of the splanchnic bed (s) has a large compliance (i.e., large volume for given height) and the other, the equivalent of the peripheral-muscle bed (p), a low compliance (smaller volume for a given height). Flow into each compartment is determined by their arterial resistances (Ra) which act like taps controlling the flows. Drainage occurs through their venous resistances (Rv) which also can be regulated. The top shows the cardiac function-venous return plot as in Figure 1. a is the system at rest and b shows what could happen with exercise. Increasing flow to the muscle bed by lowering its inflow reisistance (Ra-p), raises the pressure in this region and increases the outflow. This is seen on the cardiac function-venous return plot as a steeper slope to the venous return curve. This allows an increase in cardiac function to produce a higher cardiac output.

outflow from that region. This concept was subsequently further developed for the cardiovascular system by Permutt and co-workers [35, 36]. The venous compartment of the splanchnic circulation is much more compliant than that of the muscle vasculature [37, 38]. This makes sense from an evolutionary point of view because there is a lot more space in the abdominal region to take up volume reserves than in the actively contracting and thinner limbs. A shift of blood flow to muscle beds because of metabolic dilation with exercise thus increases net venous return. This appears on the cardiac-venous return plot as a steepening of the slope of the venous return function, which has resistance units. However, the x-intercept, which is MSFP, does not change because when flow is zero the pressures is the same everywhere in the vasculature (**Figure 2**).

Permutt and coworkers further explored the mathematical basis for this. The product of a resistance and compliance draining a vascular bed gives its time constant of drainage (τ) [35, 36]. The τ is the time it takes to get to ~63% of a new steady state pressure and volume when there is a step change in flow into a region. Based on animal studies, estimates of the τ draining the splanchnic bed are in the 20–24 second range, and those of the muscle compartment 4–6 second.

2.5 Importance of τ in the circulation

The τ for filling and draining regions in the vasculature are of great importance because pressure and flow in the system are pulsatile. This creates a periodicity that fixes times for flow into and out of vascular regions. As the frequency of cardiac pulsations increase, the τ of a region can limit flow. As a reminder, τ is the product of the compliance and resistance of a system. Since the left ventricle develops a very high elastance during ejection [39], and thus a low compliance, and it pumps into

large conductance vessels with low a low input resistance, the τ of emptying of the left ventricle is much shorter than the τ of emptying of systemic veins returning blood to the heart. However, even then, the ventricle does not eject all its volume during systole. Similarly, right ventricular filling does not normally reach the limit of filling during diastole because there is not enough time to do so. There is thus room in the system to respond to faster inflow to the right ventricle, and for the left ventricle to handle the increased volume per minute. However, as heart rate increases, diastole and systole shorten and there is less time for ejection and filling. Ejection is aided by the marked decrease in arterial resistance with exercise which shortens the τ of ejection. On the diastolic side, there needs to be a shortening of diastolic relaxation and a shortening of the period of ejection to allow more time for flow to come back. The increase in the rate of venous return is aided by the decrease in venous resistance through a number of mechanism. These include a decrease in the venous resistance of muscle because of passive dilation from higher flow as well as possible flow-mediated active dilatation and decreased resistance to the venous drainage of the splanchnic bed which is driven by beta-adrenergic activity [28, 40]. As discussed above, another factor is the distribution of blood flow between the splanchnic and muscle beds which is discussed next.

3. Two compartment computational model of the circulation and determination of maximal cardiac output

Based on the rational above, we adapted a computational model of the circulation so that it had two parallel venous compartments [41]. One compartment represented the splanchnic bed and had a τ at rest of 22 sec and the other represented the muscle compartment with a resting τ of 4 sec. Resting parameters used in the model were based on animal and human data and adjusted to give known resting hemodynamic values in humans [2, 6, 42]. These included a resting heart rate of 65 b/min, cardiac output of 5 l/min, and a mean blood pressure of 93 mmHg. Adjustments were then made in circuit parameters as needed to aim for a peak cardiac output in the range of 20–25 L/min and a mean blood pressure of 115 mmHg. Values for resistances and compliances in the model, and their changes with sympathetic activation, were based on animal studies [26–28, 36, 38, 40]. Modeling cardiac parameters turned out to be very challenging. Two critical assumptions were the limit of diastolic filling of the right heart because it sets the maximum stroke volume and second, the constants that determine the shape of the diastolic passive filling curve of the right and left ventricles because these affect diastolic filling pressure and thus the gradient for venous return. Based on values in the literature, we set the limit of a normal right ventricular diastolic volume to 140 ml. With a heart rate of 180 b/min, this gave an upper limit to the maximum possible cardiac output of 25 L/min.

To simulate the maximal exercise condition we first increased the heart rate to 180 b/min. Without any adjustments in the mechanics of the circulation this actually lowered cardiac output. Even when we shortened the systolic ejection time and the τ for diastolic relaxation of the ventricles, in the absence of adjustment other circuit factors, there still was little change in resting cardiac output. This is because blood needed to come back faster. When we increased the distribution of blood flow going to the muscle bed from 60 to 90% as expected during exercise, t cardiac output increased only moderately and arterial pressure fell markedly, which contributed to lower than expected muscle blood flow. Based on a previous study of baroreceptor regulation of the systemic circulation [28], we reduced the resistance draining the splanchnic bed as well as the capacitance of that bed to produce an increase in stressed volume of 6 ml/kg. From studies on the τ of isolated

contracting skeletal muscle [43, 44] we lowered the venous resistance of the muscle bed during the simulated exercise condition from 4 to 2 sec. Each of these individually only produced small changes in cardiac output. However, when they were all put together, and arterial resistances were adjusted to obtain the expected arterial pressure, cardiac output was still only around 17 L/min, and much less than what we were aiming for, which was 20–25 L/min. Another consequence was that the venous pressures markedly increased in the veins of muscles, which means that capillary pressures would have been markedly elevated and there would be major capillary leak.

The two compartment model and the τ draining the regions can be used to give a mathematical formulations of the maximum cardiac output:

$$Q = \frac{\gamma - \left(C_T \; x \; Pra\right)}{F_S \tau_S + F_M \tau_M} \tag{2}$$

Q = cardiac output (L/min), γ = stressed vascular volume (L), C_T = total vascular compliance (ml/mmHg, and is the sum of splanchnic and muscle compliances), F = fractional of total cardiac output to the region, τ = time constant (sec) and subscripts S and M = splanchnic and muscle vasculatures, respectively. This simplification omits the small variation that would occur if volume accumulates or is lost in the pulmonary circuit.

3.1 Muscle pump

The solution for reaching known high values of cardiac output at peak exercise was to add the equivalent of a muscle pump by having active compressions on the muscle venous compartment. This increased cardiac output to the 22–23 L/min range we were aiming for. The muscle pump acted through a number of mechanisms. The marked decrease in arterial resistance that is required to increase blood flow to the working muscle results in capillary and venous pressures that approach arterial pressure. The high venous pressure then stretches the compliant venous walls and a large amount of volume would accumulate in the muscle vasculature. This effectively creates a loss of a large proportion of stressed volume from the circuit. By forcefully squeezing veins during contraction, muscle contractions transiently empty the venous volume to almost zero. This appears as a large venous pulse of flow from the veins of contracting muscles [30, 44, 45]. Transiently lowering local venous volume also ensures that the capillary pressures do not remain persistently high when exercising and thereby reduces capillary leak. Another effect of the muscle pump is that it "speeds" up the movement of blood from the muscle veins to the heart, effectively decreasing the time constant of venous drainage [43]. The importance of this will be discussed below under factors affecting RV filling.

Muscle contractions do not send blood in the retrograde direction because of the presence of a Starling resistor-like mechanism at the arteriolar level [46]. Because of this mechanism, the muscle also does not "suck" blood from the arteries and does not act as an auxiliary pump; rather, it facilitates flow by preventing volume accumulation in the muscle vasculature. When strong enough, muscle contractions likely even pump blood through the tricuspid and pulmonary valves during systole and diastole, and thereby increase the time and the cycles for flow to go through the right heart.

A number of factors determine the effectiveness of the muscle pump. The most obvious is that the force generated must be adequate to compress the venous compartment. In the modeling study, the effect was evident with a force of 0.25 mmHg/ml. The larger the muscle groups, the larger the affect because there is more volume to empty.

4. Implications for peak performance of the observations from the modeling study

Since stroke volume is a key determinant of the maximum cardiac output, a person's innate heart size as determined by their genetic make-up is a key variable. This does not change much with training. Rather, training changes the characteristic of the kinetics of the return. This is largely related to the amount of muscle. Basic muscle mass generally evolves in proportion to heart size and these are genetically linked. Muscle mass, though, can be increased by training and this likely is what accounts for the expected potential 20% increase in aerobic power with training in someone who has not been previously active [10, 13, 47]. More muscle means that more blood can come back to the heart. If someone has already been active aerobically there likely is little more to gain in VO_2-max with training. This does not mean, though, that they cannot do more with what they have by an increase in their anaerobic threshold [48].

The importance of the amount of muscle as a determinant of cardiac output becomes an issue when trying to restore lost muscle. A question that needs to be answered for rehabilitation of lost muscle is what level of aerobic activity is needed to be to promote return of the original muscle mass? If the person's capacity starts very low, it then may not be possible to do a high enough level activity to generate the increase in blood flow in working muscle to generate an increase in aerobic activity. Age likely plays a role, too, in the capacity of muscle to recover. There are many examples of athletes with high aerobic power who have had significant injuries but still are able to return to performing at high aerobic levels. With aging though, return of full mass might be less effective despite high levels of training. There is evidence of this in recovering critically ill patients beyond age 50 [49].

Since maximum stroke volume is largely determined at birth, and does not increase to any significant degree after full growth, the fall in heart rate that occurs with aging directly impacts maximum cardiac output with aging. There can be some compensation by an increase in stroke volume because there usually are some stroke volume reserves but these are limited. In the modeling study, decreasing maximum heart rate to 160 b/min only lowered cardiac output by 2%, but lowering it to 140 b/min decreased maximum cardiac output by 16% with little further change until it was lowered to below 120 b/min.

Regulation of blood pressure during exercise turned out to be very complicated. A key variable for the increase in cardiac output was the increase in fractional flow to the muscle bed. This could occur by just decreasing the arterial resistance going to the muscle vasculature, by increasing the resistance to the non-muscle splanchnic vasculature, or by some combination of both. If the fractional flow to the muscle only was produced by decreasing the arterial resistance in that region, and without muscle contractions, arterial pressure markedly fell in the model because of the increased trapped blood in muscle veins. When muscle contractions were added, the normal volume distribution was restored and blood pressure markedly increased above expected levels. It was then necessary to decrease splanchnic resistance in the model to obtain the expected arterial pressure. Higher arterial pressures also increase the fractional flow to the muscle compartment because the time constant of inflow is much faster to muscle because of its lower arterial resistance. It is the ratio of the arterial resistances between the two compartments that ultimately counts for the slope of venous return, so we found that we had to adjust the two arterial resistances to obtain known values. Failure of compensation of the arterial resistances to the splanchnic and muscle compartments could lead to clinically significant exercise induced hypertension or even hypotension in some cases.

Additional factors: There were no atria in the modeling study. In unpublished studies we have added atrium. Under resting conditions, atrial contractions had little effect on cardiac output but with all the processes in place at peak performance, atrial contractions added as much as a 10–20% further increase in cardiac output.

Besides the muscle pump, there are two other pumping mechanisms that can increase venous return and cardiac output during exercise. The descent of the diaphragm during the vigorous respiratory efforts at peak performance can transiently raise abdominal pressure [50, 51] which will compress the splanchnic venous compartment and increase the rate of venous return from this region. In the thorax, the inspiratory fall in pleural pressure can increase venous return although this effect only can work by lowering venous pressure to atmospheric pressure. Below that the Starling resistor mechanism limits any further increase in the rate of return. Active expiration can increase intrathoracic pressure, which could aid left ventricular ejection, but this benefit is more likely offset by the positive pleural pressure decreasing venous return. The final effect would depend upon the balance of potential recruitment of volume from the splanchnic compartment versus the inhibition to flow in the thorax.

5. Conclusion

Maximum cardiac output is a key determinant of maximum aerobic performance [4]. A fundamental principle in the circular circulatory system is that what goes out per time must come back at the same rate. Thus, the maximum ejected stroke volume per beat must be matched by an equal stroke return. The determinants of stroke return often are under-appreciated in discussions of the limits of aerobic performance. I have reviewed these factors in detail based on an analysis obtained from a computational model of the mechanics of the circulation at maximal exercise [41]. The role of the muscle pump was very evident in the analysis. Besides the obvious importance of muscles for performing work, muscle contractions play an essential role in increasing cardiac output by decompressing the volume that otherwise would accumulate in the muscle venous compartment, and by speeding

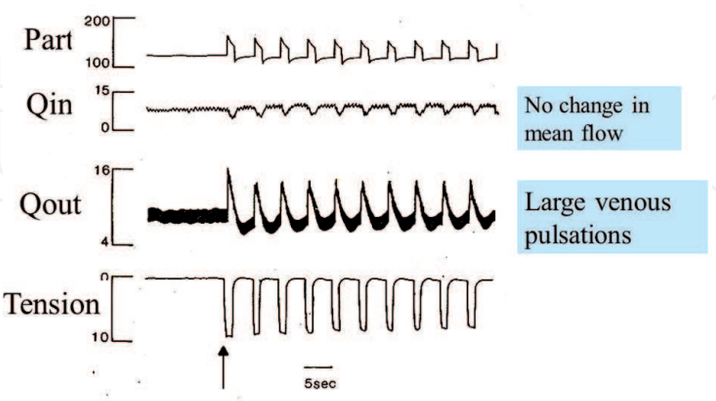

Figure 3.
Effect of muscle contractions on blood flow in isolated gastrocnemius. The gastrocnemius muscle of a dog was isolated, maximally dilated and perfused with a constant flow pump. The top line is arterial pressure (Part, mmHg), the second is inflow (Qin, ml/min measured with an electromagnetic flow probe), the third is outflow (Qout, ml/min) and the fourth the generated longitudinal muscle tension (T, gm). Muscle contractions raised arterial pressure. There was a small transient fall in Qin because the contractions obstruct flow. There are large increases in Qout with the contraction, which make it look like more total flow went out but Qin is constant so the flow is unchanged. This tracing is the same as that of Folkow et al. [52] who based on the venous pulsations concluded that muscle contractions increase muscle blood flow but they did not measure Qin which indicates that mean flow does not change. Reproduced with permission from Naamani et al. Eur J Appl Physiol 1995 [44].

up the return of blood to heart. These roles of contracting muscle in determining cardiac output and decompressing the muscle vascular beds could be a fruitful area for further investigations with implications for maximizing athletic performance, as well rehabilitating persons with reduced muscle capacity. Issues that should be important are ideal rates of contraction and force of contraction needed to have training effect. In our modeling study, increasing contraction rates from 50 to 150 contractions/minute or force of contraction of greater than 0.25 mm Hg/ml did not change cardiac output, presumably because the veins were maximally compressed, but this was an idealized assessment and treated all muscles as one. The rate and force factors could be a much more important factor in arm versus leg exercise, and in debilitated and elderly patients with limited capacity for production of muscle force.

With normal cardiac function, the heart can handle what comes back as evident by maintenance of a low Pra. However, the heart does not have volume reserves that it can use to increase rate of return to the heart by increasing MSFP. Increased cardiac output thus is very dependent upon the increased of the return function and the effect of muscle contractions. On the other side, muscle performance is very dependent upon the delivered blood flow so that flow from the muscle and into it are intricately connected for optimal performance (**Figure 3**).

Author details

Sheldon Magder[1,2]

1 Department of Critical Care, McGill University, Montreal, Quebec, Canada

2 Department of Physiology, McGill University, Montreal, Quebec, Canada

*Address all correspondence to: sheldon.magder@mcgill.ca

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