Commentary
Understanding cardiac output
Jean-Louis Vincent

Department of Intensive Care, Erasme Hospital, Université libre de Bruxelles, Route de Lennik 808, 1070-B Brussels, Belgium

Corresponding author: Jean-Louis Vincent, jlvincen@ulb.ac.be

Abstract

Cardiac output is the amount of blood the heart pumps in 1 minute, and it is dependent on the heart rate, contractility, preload, and afterload. Understanding of the applicability and practical relevance of each of these four components is important when interpreting cardiac output values. In the present article, we use a simple analogy comparing cardiac output with the speed of a bicycle to help appreciate better the effects of various disease processes and interventions on cardiac output and its four components.

Introduction

Cardiac output, expressed in liters/minute, is the amount of blood the heart pumps in 1 minute. Cardiac output is logically equal to the product of the stroke volume and the number of beats per minute (heart rate). Easy enough, one may think, but the term cardiac in cardiac output is potentially mis-leading – with clinician's sometimes assuming that to inter-pret cardiac output they must focus on the heart. The heart is just one part of the much larger cardiovascular system, however, and the amount of blood it pumps is dependent on both cardiac and extracardiac factors.

Although most clinicians should/will be able to recite the four determinants of cardiac output – heart rate, contractility, preload, and afterload – understanding of the applicability and practical relevance of each of these four components is all too often less well ingrained. To try to clarify the individual roles and the combined roles of these four factors in generating cardiac output, and hence to facilitate our understanding of the effects of disease processes and therapies on cardiac output, I use a simple analogy that equates cardiac output (that is, the amount of blood pumped by the heart over a period of time) with the speed of a bicycle at a particular time point (Figure 1).

The analogy and the four determinants of cardiac output
Heart rate
The heart rate is perhaps the simplest determinant of cardiac output to visualize: the faster the heart beats, the more blood can be pumped over a particular period of time. Using our analogy, the faster the cyclist pedals, the faster the bicycle will go. But things are not quite so simple! Staying with the bicycle analogy, it is easy to imagine that if the cyclist pedals too fast for too long, he/she will get tired and be unable to maintain the rate of pedaling, so the bicycle will slow. There is an optimal rate of pedaling: too fast and the cyclist will tire too quickly and have to slow down; too slow and the bicycle will not move fast enough to cover the required distance. Similarly, if the heart rate is too slow, usually easily identified as part of a severe bradyarrhythmia, *or* is too fast, then cardiac output can be impaired. Acute supraventricular or ventricular tachycardia may also be a cause of low cardiac output, and even of cardiogenic shock.

Contractility
Clearly, if the cyclist flexes his/her muscles a little and pushes harder on the pedals, then the bicycle will move faster. This can be equated to an increased contractility of the heart muscle, resulting in increased cardiac output. Too little pedal power, or impaired contractility, will reduce cardiac output; however, too much effort will result in fatigue, sometimes leading to a complete collapse, with the need to slow down substantially or even to stop. This may occur with excessive inotropic support, resulting in increased mortality rates.

Preload
Preload is the degree of myocardial distension prior to shortening. As initially demonstrated by Otto Frank and Ernest Starling, an intrinsic property of myocardial cells is that the force of their contraction depends on the length to which they are stretched: the greater the stretch (within certain limits), the greater the force of contraction. An increase in the distension of the ventricle will therefore result in an increase in the force of contraction, which will increase cardiac output. In our analogy, preload can be compared with a tailwind allowing the cyclist to move faster without any additional muscular effort. Of course, unlike our analogy – in which the speed of the bicycle will continue to increase as the speed of the wind increases – in the heart a preload value will

Figure 1
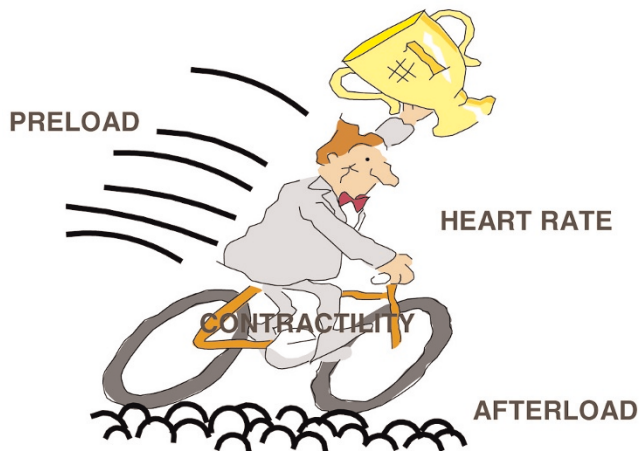
Four determinants of cardiac output, using an analogy to the speed of a bicycle.

eventually be reached at which cardiac output will no longer increase.

Preload largely depends on the amount of ventricular filling. It should not, however, be confused with the venous return. In our analogy, the venous return is like the speed of the bicycle coming towards us. The amount of blood returning to the heart in any period of time must be equal to the amount of blood pumped by the heart in the same period, as there is no place for storage of blood in the heart. Venous return therefore equals cardiac output, whereas preload is only one component of cardiac output.

Afterload
Afterload is the force against which the ventricles must act in order to eject blood, and is largely dependent on the arterial blood pressure and vascular tone. By cycling on a large smooth road rather than a narrow, bumpy one, or on a road with a gentle downhill slope, the bicycle's speed can increase significantly for a given degree of muscular effort. A tired cyclist is particularly sensitive to these aspects. Similarly, reducing afterload can increase cardiac output, especially in conditions where contractility is impaired.

Some clinical applications
Myocardial depression of sepsis
Sepsis is usually associated with a normal or high cardiac output; yet many studies have shown that myocardial depression can occur even early in the course of sepsis [1], so why is cardiac output not reduced? The pathophysiology of sepsis involves the release of cytokines, some of which are associated with abnormal calcium handling by the cardiac myocytes [2], leading to reduced myocardial contraction. Because of the simultaneous tachycardia and reduced

vascular tone, however, afterload is reduced – and cardiac output can therefore be maintained or even increased. In addition, the hyperkinetic state seen in sepsis is typically preceded by fluid therapy. This situation is akin to the cyclist being too tired to push on the pedals, but being able to keep up speed because of a smooth downward sloping road.

Deleterious effects of inotropic therapy
As the long-distance cyclist will know, prolonged strenuous exercise can lead to high tissue oxygen demands, which can later result in impaired muscle contraction and poor performance. Positive inotropic drugs act by different mechanisms to increase the contractility of the heart, and as such have been proposed for use in patients with cardiac failure to increase myocardial contractility and hence cardiac output. Indeed, in the short-term, acute phase of heart failure, inotropic drugs can be useful to increase cardiac output. When considered in light of our analogy, however, it is easy to appreciate that excessive inotropic stimulation may increase the myocardial oxygen demand, leading ultimately to myocardial ischemia. Indeed, prolonged stimulation with long-term inotropic therapy has been shown to increase mortality rates in patients with chronic heart failure [3-5]. In contrast, reducing the force of contraction may enable the cyclist to pedal longer; this may account for some of the beneficial effects of prolonged β-blockade therapy in the treatment of heart failure.

Beneficial effects of vasodilating substances
Arterial vasodilator therapy results in significant improvements in cardiac output in patients with heart failure by reducing afterload (cycling downhill). Interestingly, this therapeutic approach has been more successful than inotropic stimulation, and has been shown to reduce mortality rates in this patient population [6,7]. An obvious limitation is the decrease in arterial pressure, which may compromise organ perfusion.

Potentially harmful effects of vasopressor agents
In contrast to the beneficial effects of vasodilator drugs, the administration of strong vasopressors may decrease cardiac output by increasing afterload, even in individuals with normal cardiac function. This effect is seen, for example, with phenylephrine, which has almost pure α-adrenergic effects. Vasopressin may also decrease cardiac output by increasing vascular tone [8-10]. Considering our analogy, this effect may be expected – increasing the slope of the road, or making the surface too uneven, will eventually force most cyclists to get off their bicycles and walk, thus reducing their speed considerably!

Even norepinephrine, which has some β-adrenergic properties, may decrease cardiac output in the absence of a reduction in vascular tone. The cyclist is pushing a bit harder on the bicycle's pedals, but as the road is now going uphill the bicycle's speed may decrease considerably. High doses of norepinephrine have been used as an experimental model of heart failure [11-13].

Effects of inodilating substances

Some drugs, such as phosphodiesterase inhibitors (milrinone, enoximone) and levosimendan, exert some inotropic effects in addition to vasodilating effects. This is analogous to pushing a bit harder on the bicycle's pedals at the same time as you pass the top of a hill and the road starts to go down again; the greater exertion may lead to fatigue, but the downhill slope helps to maintain speed. This is why these agents may increase myocardial oxygen requirements less than other inotropic drugs.

Effects of fluid administration

Fluid administration takes advantage of the Frank–Starling relationship to increase stroke volume and cardiac output. Although an excessive increase in the end-diastolic volume may increase myocardial oxygen requirements, this intervention is associated with relatively limited consequences, as compared with catecholamines. Fluid administration is like adding a tailwind to the cyclist.

Effects of calcium entry blockers on cardiac output

As calcium is essential to myocardial contraction, calcium entry blockers are expected to decrease the force of contraction of the myocardium. This is observed in isolated myocardium, but not in living organisms, where the simultaneous decrease in vascular tone (especially with the dihydropyridine derivatives) helps to maintain and even increase cardiac output. The cyclist is tired, but the road is smoother, with a gentler upward slope!

Conclusion

The interpretation of cardiac output is not as straightforward as it may seem at first glance. Comparing the complex relationship of cardiac output and its four components with the speed of a bicycle and its determinants, however, can help us to understand some of the complex pathophysiological alterations in critical illness and to appreciate better the effects of various interventions on cardiac output.

Competing interests

The author declares that they have no competing interests.

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