The cardiovascular effects of aortic clamping and unclamping

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This narrative review is intended to describe the cardiovascular pathophysiology and management of aortic clamping and unclamping.

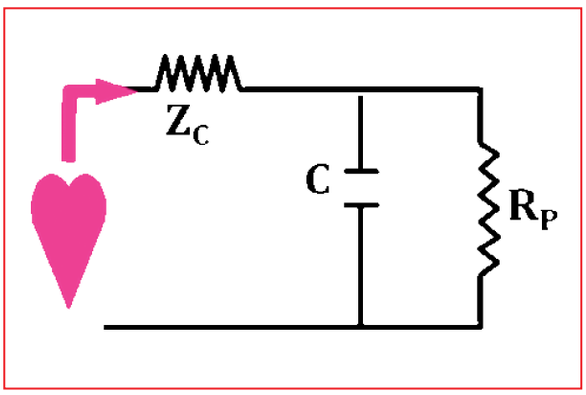
Background physiological considerations

It is common knowledge that afterload increases on aortic clamping. Afterload is defined as the force that opposes shortening of the myocardial fibres. While afterload is usually considered to be as the forces outside (extrinsic to) the ventricle, it should also be regarded as those forces intrinsic to the myocardium that oppose myocardial fibre shortening.

Afterload extrinsic to the ventricle

The most common descriptor of afterload in the clinical setting is peripheral vascular resistance. Nonetheless, this is only one of the elements of afterload. A comprehensive descriptor of left ventricular extrinsic afterload is contained in the 3-element Windkessel (wind-chamber) model. Although this Windkessel circulatory model contains only characteristic impedance, aortic compliance and peripheral (systemic) vascular resistance, it can accurately reflect all the forces that comprise afterload external to the ventricle.Using an electrical analogue of the Windkessel model, afterload can be described mathematically (Equation 1). Inspection of this equation reveals that impedance is a complex, frequency dependent parameter. The frequency dependent component is a result of wave reflections that originate at arterial and arteriolar branches.

Figure 1. Windkessel electrical analogue model of the circulation



$$Zin(\omega) = Zc + (Rp / (1 + j\omega C\ Rp))$$

Equation 1

Where Zin(ω) is input impedance at a particular frequency; Zc is characteristic impedance; Rp is a peripheral resistance element; j is the square root of -1; C is compliance.

$$Ea = R_{total} / (ts + \tau(1 - e^{-td/\tau}))$$

Equation 2

Where Ea is effective arterial elastance; R total is the sum of all resistances; ts is systolic time; td is diastolic time; τ is the time constant of the diastolic decline in aortic pressure.

It is not important to remember these formulae, but they are reproduced for the reader to appreciate the factors determining afterload.

Effective arterial elastance (Ea) is a simple descriptor of afterload that takes all the complex elements of impedance into account. For the purposes of this discussion, there are two applications of Ea. Firstly, although Ea can be calculated using a complex formula (Equation 2), Ea can also be simply calculated as ratio of end-systolic pressure (equivalent to mean arterial pressure) and stroke volume. This means that a parameter that truly reflects impedance can be measured in the clinical setting if stroke volume and mean arterial pressure are known. Secondly, Ea can be easily superimposed on a pressure volume diagram. An increase in the slope of the Ea line represents an increase in afterload. This graphic relationship can

be easily manipulated to improve appreciation of changes in afterload.

Note that all descriptors of afterload external to the ventricle consider pressure and flow. In the clinical setting, it is preferable to primarily manage pressure and flow, rather than focus on treating vascular resistance.

Afterload "intrinsic" to the ventricle

The force opposing shortening of muscle fibres within the ventricle is called wall stress-tension (Equation 3).

Wall stress $\sigma \cong \approx$ Pr/h

Equation 3

where P is the pressure generated by the ventricle; r is the radius of the ventricle and h is the wall thickness thereof.

Note that these parameters are not static and a pressure-stress loop can be created as ventricular pressure, volume and thickness vary during the cardiac cycle. For the purposes of this discussion, two factors regarding wall tension are of relevance.

1. Wall tension or stress is a major determinant of both myocardial oxygen supply and myocardial oxygen demand. An increase in wall stress increases demand and decreases oxygen supply, particularly in the subendocardium. This may result in myocardial ischaemia, particularly in the presence of overt coronary artery disease.

2. The radius of the ventricle influences wall tension. In other words, increases in preload will increase afterload, and deleteriously affect myocardial oxygen supply and demand.

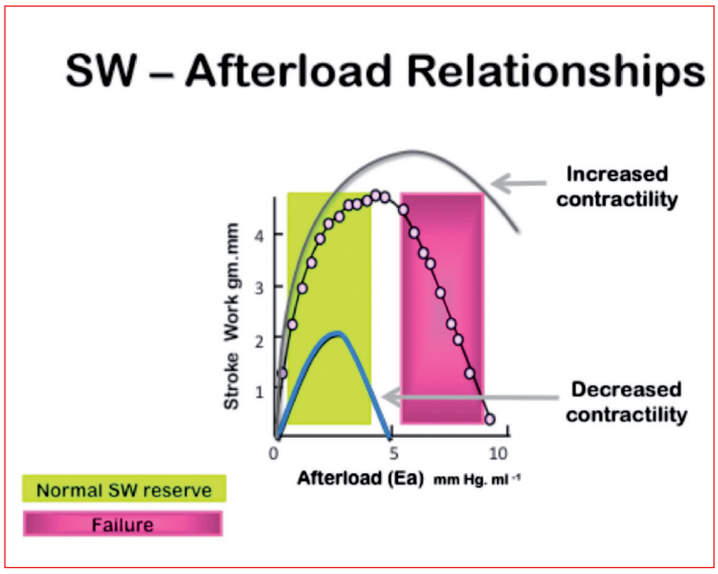
Coupling of the ventricle to its load

Afterload should not be seen in isolation, but related to the ability of the ventricle to contract. For the purposes of this discussion, there are two valuable and informative representations of coupling.

1. The **parabolic relationship between left ventricular stroke work and afterload** (Figure 2) is a useful representation of coupling. Normal left ventricles usually function on the left bottom part of this relationship. This means that, as stroke volume and arterial pressure increase (for example as the subject exercises), stroke work (effectively the product of stroke volume and pressure) can increase. The descending limb of the stroke work-afterload relationship can be appreciated as if it is considered that stroke volume decreases as afterload increases; ventricles on this part of the stroke work-afterload relationship can be considered to be failing. Two further points are valuable when looking at this relationship. Firstly, there is a family of curves relating stroke work to afterload depending on the contractile state of the ventricle. An increase in contractility shifts the relationship up and to the right; in other words, a ventricle with greater contractility can cope with a greater afterload before it fails. The converse also applies. Secondly, ventricular efficiency is maximal when it is on the upslope of the stroke work-afterload relationship. Ventricular efficiency falls markedly thereafter.

2. The **left ventricular pressure volume loop**, with Ea and end systolic elastance (Ees) lines superimposed on it, is a useful and intuitive descriptor of coupling. This relationship can be manipulated to describe what happens to left ventricular stroke volume, end-diastolic volume, ejection fraction and efficiency as Ea and Ees change. Again, two relevant points are that normal contractility is represented by a steep Ees relationship, and that the [absolute value] of the Ees/Ea relationship is a useful indicator of coupling. For further discussion of this topic, the interested reader is referred to discussions by Sagawa, Sunagawa and Maughan.

Figure 2. The parabolic relationship between stroke work and afterload. The upper grey and lower blue relationships represent increases and decreases in contractility, respectively



Cardiac and vascular pathophysiology of aortic clamping

The instinctive approach that clinicians have to aortic clamping is that afterload and blood pressure increase, and cardiac output and stroke volume decrease. While this predictable phenomenon has been demonstrated in many studies, other researchers have demonstrated no decrease or even an increase in cardiac output. The contradictory results have arisen because research has often been conducted on healthy animals without coronary artery disease, which does not consider the concomitant pathology that accompanies human vascular disease. There are five predominant factors that the anesthesiologist must take into account when considering the possible haemodynamic consequences of aortic clamping:

1. Increase in left ventricular afterload
2. Left ventricular function
3. Presence of coronary artery disease and myocardial ischaemia
4. Preload increases that can accompany aortic clamping
5. Wall tension

The abovementioned factors will be dealt with individually, albeit they interact with each other.

The degree of the increase in afterload

The degree of increase in afterload is dependent predominantly on two factors.

1. **The level of clamping**. The more proximal the position of the aortic clamp, the greater the increase in afterload. After low, infrarenal clamping, afterload decreases by only 5 - 7% (Table I). This has few consequences in patients with otherwise normal left ventricles. With higher (suprarenal and supracoeliac) clamping, the greatest increases in afterload are seen with substantial increases in afterload, leading to significant decreases in both stroke volume and ejection fraction. Severe increases in afterload are associated with ventricular dilation and subendocardial ischaemia.

2. **Aorta occlusive or dilated disease**. Patients with aortic occlusive disease have the greater peri-aortic collateralisaton, with the smallest increases in afterload following clamping of the aorta.

Contractility

The normal left ventricle has a steep Ees relationship and considerable ability to deal with increases in afterload. The performance of the normal left ventricle is therefore, within limits, afterload independent. This implies that small to moderate increases in afterload are easily tolerated by the normal left ventricle, with little decrease in stroke volume.

Should the afterload increase significantly, as will occur with clamping of the descending aorta, even a normal left ventricle will "fail". However, a poorly contractile ventricle that is presented with even moderate increases in afterload will also fail. A problem with the description of cardiovascular effects of aortic clamping is the paucity of objective information on the consequences of aortic clamping in the presence of poor left ventricular function. Therefore, basic principles of cardiac pathophysiology must be applied in these situations. The potentially deleterious effects of (excessive) beta blockade on myocardial contractility and the interaction thereof with aortic clamping have, to the best of our knowledge, not been described.

The Anrep effect

Almost 100 years ago, Anrep observed the partial recovery over time of left ventricular dilation that follows acute aortic constriction. This recovery of end-diastolic volume and pressure toward control has

Table I.

Cardiovascular Variable	Percentage (%) Change in Occlusion			
	Descending Thoracic Aorta	Supracoeliac	Suprarenal-Infracoeliac	Infrarenal
Mean arterial blood pressure	35 – 84 ↑	54 ↑	5 – 10 ↑	2 ↑
Pulmonary capillary wedge pressure	90 - 190 ↑	38↑	10 ↑	0
CVP	35 ↑			
Cardiac index	29 ↓		10 – 33 ↓	
End-diastolic area		28 ↑	2 ↑	9 ↑
End-systolic area		69 ↑	10 ↑	11 ↑
Ejection fraction		38 ↓	–10 ↓	–3 ↓
Patients with wall motion abnormalities		92 ↑	33 ↑	0

Adapted from Roizen et al

been interpreted as being a positive inotropic effect. The increase in contractility following the increase in afterload may be due to increases in coronary blood flow that accompany increases in aortic pressure or time dependent recovery of autoregulation within the coronary vascular bed. Observations documenting that the Anrep effect is associated with epicardial to endocardial redistribution of blood flow supports the notion that recovery from ischaemia is the main mechanism of the Anrep effect. Despite the widely held belief that the Anrep effect is useful to ameliorate the increase in left ventricular afterload that accompanies aortic clamping, it cannot in practice be relied on, as its existence under anesthesia has been questioned.

Increase in preload accompanying aortic clamping

Marked increases in preload are seen in response to aortic clamping. The higher the clamp, the greater the observed increase in preload. The increase in preload is seen as increases in left ventricular end-diastolic volumes and pressures. The pathophysiological reasons put forward for the increase in preload are, firstly, blood volume redistribution theory and, secondly, that afterload induced increases in preload.

One hypothesis that has been proposed to explain the increase in preload in response to aortic clamping is referred to as the ***blood volume redistribution theory***, which encompasses passive arterial and active venous components.

The hypothesis proposes that, with application of the aortic cross clamp, the passive elastic recoil of the arterial vessels distal to the clamp results in a volume of blood being expelled into the circulation. The higher the clamp, the greater the volume of blood expelled. The autotransfused volume is greater with higher clamping, particularly when the aortic cross clamp is above the splanchnic vasculature.

Another important component of the blood volume redistribution theory is based on the interaction of sympathetic outflow below the level of the clamp and accompanying splanchnic venoconstriction. The normally very compliant splanchnic vasculature acts as a functional blood volume reservoir that, depending on the prevailing sympathetic tone, can acutely attenuate both increases and decreases in blood volume. On the one hand, the normal large compliance of the splanchnic vasculature results in it being able to assimilate increases in blood volume. On the other hand, the increase in sympathetic tone and venoconstriction accompanying acute hypovolaemia can result in rapid return to the circulation (autotransfusion) of the approximately 25% (800 ml) of the blood volume usually contained in the splanchnic venous system.

The release of noradenaline and adrenaline that accompanies supracoeliac-aortic clamping decreases splanchnic venous capacitance, and may fail to ameliorate or even aggravate the autotransfusion from both the splanchnic vasculature and from the non-splanchnic vessels distal to the clamp. Support for the blood volume redistribution theory comes from animal models, in which simultaneous clamping of the aorta and inferior vena cava prevented the associated increase in preload.

There would appear to be an interaction between the level of the clamp and the blood volume redistribution theory. With infrarenal clamping, there is less autotransfusion due to elastic recoil of the arterial tree, and also less venoconstriction of the splanchnic bed. The interaction of these factors tends to ameliorate any blood volume redistribution that would accompany infrarenal aortic clamping. However, supracoeliac clamping will result in significant autotransfusion.

A further factor increasing preload has been referred to as **afterload recruitable increases in preload**. A normal response of the left ventricle is to dilate in response to increases in mean arterial pressure. This dilatation may be minimal in normal hearts with normal contractility facing a small increase in afterload. However, the greater the increase in afterload and the poorer the ventricular contractility, the more the ventricle will dilate. This mechanism may represent a teleological attempt to limit the afterload associated decrease in stroke volume.

Decreased left ventricular compliance and/or diastolic dysfunction can aggravate the consequences of the increase in preload on the left ventricle.

Wall tension and aortic cross-clamping

From the introductory discussion of afterload, it is apparent that an increased left ventricular radius will increase left ventricular wall tension, and result in or aggravate myocardial ischaemia.

Coronary blood flow and myocardial ischaemia and aortic clamping

Even in the absence of coronary artery disease, the increases in preload and afterload accompanying aortic cross-clamping lead to increases in both myocardial oxygen demand and limitation of (subendocardial) myocardial oxygen supply. Buckberg demonstrated that, in dogs without coronary artery disease, cross-clamping of the descending thoracic aorta was accompanied by a greater than 70% increase in myocardial oxygen consumption and in coronary blood flow. Clamping of the descending

thoracic aorta has been associated with decreases in phosphoro-organic compounds and intracellular pH, indicating the presence of myocardial ischaemia in a dog model with normal coronary arteries.

Hertzer and colleagues performed cardiac catheterisation on 1 000 consecutive vascular surgery patients, and described a high incidence of angiographically identifiable coronary artery disease. The response to aortic clamping in patients with coronary artery disease differs from that seen in animal models, in which the coronary artery anatomy is normal. In patients with coronary artery disease, filling pressures increase, unlike the decrease seen in the presence of normal coronary arteries. Regional wall motion abnormalities are frequently seen during clamping. Even with infrarenal clamping, patients with significant coronary artery disease will develop myocardial ischaemia. Furthermore, the left ventricular systolic and diastolic dysfunction accompanying the development of myocardial ischaemia will aggravate ventricular dilation associated with aortic clamping. A vicious circle of left ventricular dilation, increase in wall tension and myocardial ischaemia may be initiated.

Baroreceptor activation in response to increase in aortic pressure will tend to decrease heart rate in response to aortic clamping and limit myocardial ischaemia. Nonetheless, what is not described by Hertzer or others is the presence of fragile atherosclerotic plaques which may be vulnerable to rupture following the haemodynamic stresses of aortic clamping.

Duration of clamping

With progressively longer durations of aortic cross-clamping, systemic vascular resistance increases and cardiac output decreases. While the reasons are not clear, they may include blood volume decreases as a result of hydrostatic pressure-induced transcapilliary fluid shifts, and release of vasoactive substances.

The sum of the effects of aortic cross-clamping

- Clamping of the **descending thoracic** aorta results in increased mean arterial, central venous, mean pulmonary arterial, and pulmonary capillary wedge pressures, and decreases the cardiac index. A two-fold increase in blood flow through the upper part of the body is a typical experimental observation.

- **Supracoeliac** aortic cross-clamping increases mean arterial pressure and pulmonary capillary wedge pressure. Echocardiography reveals decreases in ejection fraction, increases in end-diastolic area and wall motion abnormalities indicative of myocardial ischaemia in the majority of patients. Suprarenal clamping level causes similar, albeit smaller, cardiovascular changes.

- **Infrarenal** aortic clamping is associated with only minimal changes and no wall motion abnormalities.

- Patients with poor left ventricular function, severe coronary artery disease, ischaemic mitral regurgitation, aneurysmal disease and a high (thoracic) application of the cross-clamp without mechanical diversion are typically at risk of a decrease in cardiac output, ventricular dilation and myocardial ischaemia.

- Haemodynamic consequences of occlusion of the aorta during endovascular repair are usually transient.

Mitral and aortic valve disease

Mitral incompetence due to existing papillary muscle dysfunction and also aortic incompetence can present significant problems, due to the increase in arterial pressure and afterload associated with aortic clamping. Mitral incompetence can also present for the first time during clamping if papillary muscle ischaemia develops. The discussion of concomitant valvular disease is beyond the scope of this manuscript.

The circulation proximal to the clamp

After clamping the descending thoracic aorta, blood flow to organs proximal to the clamp doubles, oxygen consumption halves and mixed venous saturation increases. Reasons for this reduction in oxygen consumption by the tissues proximal to the clamp are not currently clear, but may be attributed to the substantial increase in sympathetic tone that accompanies aortic cross-clamping. Sympathetic simulation and norepinephrine infusions decrease capillary density, tissue oxygen extraction and oxygen uptake. The substantial arteriovenous shunting that occurs in the upper body after descending aortic clamping is best explained by the accompanying increases in blood pressure. The decrease in renal and, potentially, spinal cord blood flow is beyond the scope of this article.

Blood loss during clamping

Blood loss during clamping, from the lumbar arteries, can be significant. Many anaesthesiologists are surprised by the sudden blood loss after the aneurysm is opened. Back-bleeding from the lumbar vessels may furthermore compromise spinal cord blood flow and has been associated with spinal cord ischaemia.

Management of clamping

The relationship between pre-surgery left ventricular contractility and increases in afterload and preload, the tendency of to the ventricle to dilate, the propensity to develop myocardial ischaemia, and the height of the clamp need to be managed acutely. It is of paramount importance that these considerations form part of the anaesthesiologist's pre-operative evaluation of the vascular patient.

Currently, strategies for myocardium preservation during aortic cross-clamping consist of decreasing afterload and normalising preload, coronary blood flow and contractility. During descending thoracic clamping, various forms of bypass or shunt are useful. However, just prior to and during lower aortic cross-clamping, vasodilators represent the main method of achieving these goals because:

- The increase in venous capacitance decreases preload;
- Afterload is reduced; and
- Coronary vasodilatation with increase in coronary blood flow and improvement of the endocardial-epicardial blood flow distribution occurs. This results in improvement in myocardial performance.

Vasodilators that can and have been employed include nitric oxide donors such as nitroprusside and nitroglycerine, calcium channel blockers such as nicardipine and magnesium, epidural anaesthesia and volatile anaesthesia agents. The details of the pharmacology of these agents are beyond the scope of this article.

The powerful "balanced" arterial and venous dilator sodium nitroprusside has been administered particularly prior to descending aortic clamping. In both patients with coronary artery disease (Attia) and normal dogs (Buckberg), reversal of myocardial ischaemia following descending thoracic aortic cross-clamping has been reported after nitroprusside administration. Albeit a potentially useful drug, sodium nitroprusside can initiate problems, such as an increased pulmonary shunt fraction with arterial hypoxaemia during one lung ventilation (during thoracic aneurysm repair), coronary steal, tachycardia, and the effects of the cyanide metabolites of sodium nitroprusside that are particularly difficult to excrete if renal dysfunction is present after descending thoracic aortic cross-clamping. Sodium nitroprusside also has deleterious effects on cerebrospinal fluid pressure, spinal cord perfusion pressure and spinal cord blood flow.

Nitroglycerine is a commonly utilised dilator with significant advantages. Unlike sodium nitroprusside, nitroglycerine does not increase heart rate nor initiates coronary steal, and it is associated with few toxic effects. It is effective at managing many of the pathophysiological effects of aortic cross-clamping. Nitroglycerine is useful in preventing and managing myocardial ischaemia associated with aortic clamping.

- At low dosages, nitroglycerine is predominantly a venodilator and is effective at minimising myocardial ischaemia primarily due to decreases in preload and wall tension. This perspective is supported by aortic cross-clamping in animals with drug-induced myocardial depression that was associated with a decrease in myocardial blood flow and in endocardial-epicardial blood flow ratios. Nitroglycerine preserves the endocardial-epicardial flow ratios above 1. An endocardial-epicardial flow ratio below 1 indicates greater subendocardial ischaemia. The authors concluded that, because coronary vascular resistances were not altered, the benefits probably accrued from decreased ventricular wall tension.
- Nitroglycerine can improve coronary blood flow during aortic clamping to reflect the greater demand for oxygen.
- While nitroglycerine does not appear to prevent myocardial ischaemia, should ischaemia develop, nitroglycerine is useful in treating regional wall motion abnormalities.
- Low dosages of nitroglycerine are not associated with increases in heart rate, particularly with concomitant beta-blocker administration.

In higher dosages, nitroglycerine also results in arteriolar dilation, decreases vascular resistance and increases cardiac output, particularly in dogs with impaired left ventricular function.

In a recent editorial, James suggests "that there is a strong argument for magnesium to be the first-line agent for management of intra-operative hypertensive events". The advantages of magnesium for management of clamping of the aorta include that it is a functional calcium channel blocker and alpha-1 blocker. James suggests magnesium is predominantly an arteriolar dilator and has minimal venodilator effects.

Recent research by Soltani and colleagues indicates that the vasodilator effects of magnesium are endothelium dependent, and are blocked by inhibitors of the nitric oxide pathway. It may be that at least part of the vasodilator effects of magnesium are mediated via the nitric oxide pathway. Albeit magnesium is beta-agonist permissive, the combined effects of prior beta-blockade and subsequent boluses of magnesium on contractility and conduction have yet to be determined. Other advantages of magnesium that are relevant to aortic surgery include improvement

in diastolic function and anti-arrythmic effects in the presence catecholamines, an analgesic effect when used as an intra-operative infusion and its NMDA-receptor antagonism that may be of benefit when the spinal cord is threatened. Magnesium does not appear to have many of the deleterious effects of sodium nitroprusside associated with clamping of the descending thoracic aorta.

Volatile anaesthetic agents have been used to facilitate aortic clamping, as they decrease aortic pressure. Isoflurane causes significant vasodilatation in dosages exceeding one MAC. This overrides its myocardial depression and results in coupling and cardiac output being maintained. Unfortunately, volatile anaesthetics also decrease myocardial contractility. It is inadvisable to use isoflurane as the (sole) vasodilator as it results in significant decreases in myocardial efficiency. Furthermore, it can induce coronary steal in dosages exceeding one MAC in the presence of hypotension if steal-prone anatomy is present. Its use in high dosages may also be associated with an increase in heart rate. Additional concerns are the as yet undescribed effects of the concomitant administration of beta-blockers and high dosages of inhalation agents on myocardial performance in the presence of acute increases in afterload. The use of isoflurane as sole agent to control haemodynamics, particularly in high aortic clamping, is probably inadvisable.

Nonetheless, the use of inhalation agents during aortic surgery may have advantages in terms of myocardial ischaemia. It is noteworthy that collateral-dependent myocardial blood flow is increased two- and three-fold by halothane and sevoflurane, respectively. In addition, these agents are not associated with increases in heart rate or a propensity to induce coronary steal, they reduce platelet adhesion and aggregation, and also induce pharmacological preconditioning in the event that myocardial ischaemia should occur. When combined as part of a balanced anaesthetic, they cause only insignificant myocardial depression. Around the period of clamping and unclamping, it is prudent to maintain an appropriate, constant anaesthesia depth, and use other means to control haemodynamics.

In this respect, if inotropic support was needed before aortic clamping, it is advisable to maintain it during clamping, particularly if inodilators are being used. Administering or being ready to adminster inotrope may be valuable if the left ventricle is already dilated, has poor contractility and a “high” clamping is anticipated. Arterial blood pressure is not the only endpoint of haemodynamic management during aortic cross-clamping. Indeed, inodilators such as milrinone have been successful by themselves to control the haemodynamic effects of aortic clamping.

Thoracic epidural local anaesthesia can ameliorate the haemodynamic response to aortic clamping.

- The increase in sympathetic outflow to the splanchnic vessels that accompanies aortic clamping is re-duced. Splanchnic venous capacitance increases. The vascular bed becomes a passive reservoir, the filling of which can be manipulated by tilting of the patient’s legs (reducing the extent of the vascular bed and causing autotransfusion) or changing the patient’s position. Thus, just prior to clamping, the patient is tilted feet down to decrease venous return.

- Myocardial oxygen supply, particularly to stenotic coronary arteries but also to non-stenotic coronaries, is increased. However, coronary blood flow to collateral dependent arteries is not improved, probably because flow in these areas is pressure and heart rate dependent.

- Myocardial oxygen demand is decreased by thoracic epidural anesthesia.

In the period after induction and prior to cross-clamping, attention needs to be paid to judicious fluid administration. Hypovolaemia and lack of compensation for anaesthesia- and epidural-associated vasodilatation, with inadequate cardiac output and hypotension, may compromise renal, gut and other organ function. Indeed, provision of adequate cardiac output and oxygen delivery prior to the period of ischaemia has been associated with improved peri-operative outcomes. However, excessive fluid administration can result in significant increases in preload and wall tension after clamping.

Furthermore, the current consensus on abdominal (non-vascular) surgery appears to be that limiting fluid administration, particularly crystalloids, is associated with reduced postoperative morbidity and mortality. While not specifically studied, this may be applicable to vascular surgery, and is practiced by many vascular anaesthesiologists.

Mechanical reduction in afterload using cardio-pulmonary bypass and distal perfusion techniques are the most appropriate techniques when clamping the descending thoracic aorta. Vasodilators can be used as adjuncts to mechanical afterload reduction, if deemed necessary.

In practice, around the period of clamping, I maintain appropriate, constant anaesthesia depth. Inhalation agents, particularly sevoflurane, are appropriate when utilised as part of a balanced anaesthesia technique. A thoracic epidural catheter is placed pre-operatively, and local anaesthetic is administered prior to clamping the aorta. In the period before clamping, judicious

fluid administration is prudent to avoid increases in wall tension on aortic clamping.

Titration of (intravenous) beta-blockers should aim for heart rate control appropriate to the patient's underlying cardiac pathophysiology. Around the time of aortic clamping and unclamping, venous return is manipulated by fluid restriction and by positioning the patient slightly feet down. The circulation and coronary blood supply and demand relationship are manipulated with vasodilators just prior to placement of the clamp. For infra or suprarenal infracoeliac clamping, a 25 - 500 µg bolus of nitroglycerine usually suffices when the above adjunctive techniques are used. However, before supracoeliac clamping, a bolus of magnesium (30 - 45 mg/kg) is administered prior to the nitroglycerine. The dosages of the vasodilators are limited or omitted when bypass or shunts are employed. Inotropic support is continued around the period of clamping.

Pathophysiology of unclamping

In the 1960s, unclamping of the infrarenal aorta was associated with a 10% mortality rate and a significant incidence of cardiac arrest. This is not currently the case. Unclamping of the aorta has been referred to as declamping shock, which represents a useful way of thinking. Reductions in arterial blood pressure (42 - 60%) and systemic vascular resistance (70 - 80%) occur, which are due to vasodilation below and above the clamp.

Below the clamp, the maximally vasodilated ischaemic vasculature (commonly termed "reactive hyperaemia") contributes to decreases in afterload (distributive shock). This is responsible for a four-fold increase in distal aortic and lower limb flow after aortic unclamping. An increase in venous capacitance, with sequestration of blood in the vessels distal to an aortic occlusion, causes reduction in venous return (functional hypovolaemia) during unclamping.

The vasculature above the clamp is subjected to vaso-active substances that cause vasodilation, damage the endothelial glycocalyx, and result in transudation of fluid into the interstitium. The release of cytokines and endotoxin from ischaemic leaky bowel causes myocardial depression (cardiogenic and septic shock). Acute myocardial ischaemia or infarction, that occurs immediately or shortly after unclamping, may also contribute to the "shock" state. This may be due to the combination of hypotension and increases in heart rate in the presence of stenotic coronary lesions and collateral dependent areas of the myocardium, or haemodynamic stresses causing plaque rupture. Increases in wall tension due to fluid administration may aggravate ischaemia.

Although the literature reports that an increase or no change in cardiac output occurs, it is our experience that cardiac output increases significantly in response to the decrease in afterload. Cardiac indices of 3,5 – 5,5 l/min/m^2 are not uncommon, depending on the extent of the area that was ischaemic, peri-aortic collateralisation and the duration of the period of ischaemia. Restoration of blood volume prevents significant reductions in blood pressure and cardiac output after unclamping in dogs and humans. However, too aggressive fluid administration can lead to complications such as myocardial ischaemia and pulmonary oedema.

Other factors may have an effect on haemodynamics after aortic unclamping:

- Oxygen radical formation, reperfusion injury and repayment of the oxygen.

- The inflammatory response, which includes:
  - Anaphylatoxin release and complement activation;
  - Prostaglandin release;
  - Platelet and neutrophil activation;
  - Release of myocardial-depressant factors, endotoxins, and cytokines.

- The lung and reperfusion:
  - Pulmonary hypertension and right ventricular dysfunction may occur.
  - Hypercarbia and acidosis may necessitate an increase in alveolar ventilation.
  - Unclamping of the aorta is associated with significant, transient increases in carbon dioxide release, and in oxygen consumption.
  - The increase in oxygen consumption may lead to mixed venous desaturation. Combined with the pulmonary low ventilation units, this may lead to arterial hypoxaemia. This may be particularly apparent if, during thoracic aortic aneurysm repair, only the right lung is being ventilated.
  - Pulmonary capillaries may become leaky, and contribute to decreased pulmonary compliance and even more overt signs of alveolar oedema, such as a reduction in arterial oxygen tension.

- The kidney:
  - Activation of the renin-angiotensin system, resulting in an increase in renin activity during cross-clamping of the abdominal and suprarenal aorta. The latter is readily explained by a decrease in perfusion pressure in the afferent arterioles. The reasons for an increase in renin activity during infrarenal aortic cross-clamping are less clear. Beta-blockade reduces

the increase in renin activity.
- Renal perfusion pressure is important to maintain renal blood flow and elimination of cytokines.

- Significant haemorrhage following unclamping may occur at suture lines.

- Hyperkalaemia can give rise to significant arrhythmias and even cardiac arrest, particularly if a too-long occluded limb is revascularised.

In summary, the main reasons for unclamping hypotension include:

- Hypovolaemia caused by the pooling of blood into reperfused tissues distal to the aortic occlusion.

- Ischaemia-mediated vasodilation, with a subsequent increase in vascular (venous) capacity in the extremities below the occlusion.

- Accumulation of vaso-active and myocardial-depressant metabolites

Prevention of unclamping shock-hypotension includes the shortest possible aortic cross-clamping time, careful titration of fluid and vaso-active drugs, and slow release of the clamp.

Management of unclamping

Preparation for unclamping should commence approximately 10 minutes before aortic cross-clamp removal. Communication between surgeon and the anaesthesiologist is important. Classically, the surgeon announces the time of the impending event with an accuracy inversely related to his/her experience. The wellbeing of the patient can, on occasion, depend on the surgeon's capacity to remove the cross-clamp in a controlled fashion and (partially) reapply it or digitally compress the aorta.

The classic approach to prevent unclamping hypotension-shock is to administer fluid before unclamping in order to increase pulmonary artery wedge pressure (PAWP) or central venous pressure (CVP) 2 - 4 mmHg above baseline. This approach is aimed at increasing cardiac output to compensate for the distal reactive hyperaemia and acute increase in the capacity of the vasculature. The classic approach further suggests that, should fluid not be sufficient to restore or maintain blood pressure, vasopressor and/or inotrope use may be considered.

We are of the opinion that a balanced approach to unclamping hypotension is needed. Firstly, judicious fluid administration should precede aortic unclamping. While approximately 5 - 15 ml/kg lean body weight of blood or colloids is reasonable, the volume administered should always consider left ventricular systolic and diastolic function and the extent of and duration of time the tissue has been ischaemic. To ameliorate increases in wall tension that invariably accompany rapid fluid administration, low dose nitroglycerine is administered concomitantly during fluid administration. The nitroglycerine infusion is terminated two to three minutes before unclamping. Leg elevation just prior to unclamping can augment venous return and "shortens" the venous system that needs to be filled. Secondly, vasopressor and/or inotrope use at the time of unclamping will ameliorate the significant decrease in blood pressure that can even trespass the lower limit of autoregulation and compromise cerebral, cardiac and renal blood flow.

Management *at the time* the aortic clamp is being removed is primarily focused on maintaining mean arterial pressure. This is best achieved by administration of vasopressors such as phenylephrine and vasopressin or its analogues. While the aim is to administer sufficient vasopressors to maintain an adequate mean arterial pressure, it is interesting to speculate that phenylephrine may cause preferential vasoconstriction in the previously non-ischaemic vascular beds that were proximal to the clamp. This could conceivably further reduce blood flow to tissues above the aortic clamp, while preferentially directing the cardiac output to the ischaemic bed. Vasopressin in combination with a significantly lower dose of phenylephrine, may result in a more balanced distribution of flow between the ischaemic and non-ischaemic vascular beds.

In the period after aortic unclamping, the focus should be on maintaining arterial pressure by ensuring, firstly, that cardiac output is adequate. Adopting the aforementioned approach implies achieving an adequate and appropriate cardiac output, using judicious dosages of inotropes and volumes of fluid or blood. Thereafter, vasopressor administration is titrated to achieve the desired mean arterial pressure. The classic approach is to administer fluid before and after removal of the aortic cross-clamp, guided by filling pressures, in an attempt to maintain an adequate blood pressure. The modified approach is guided by monitoring cardiac output.

Colloids, particularly the synthetic starches, have been shown to decrease capillary leak, leucocyte adherence and transmigration in the presence of inflammatory mediators. The clinical significance thereof can be seen in the better oxygenation observed by Rittoo and colleagues in research in vascular surgery patients. Nonetheless, maintenance of adequate glomerular filtration demands that colloid osmotic pressure not

be significantly increased. Furthermore, it is probably unwise to increase serum chloride levels significantly in patients with threatened renal function. Therefore, Ringer's lactate may be administered in conjunction with colloid solutions. Inspection of left ventricular contractile status and end-diastolic volume using transoesophageal echocardiography is becoming an increasingly accepted adjunctive monitoring modality in aortic surgery.

It has been suggested that inhalation agent concentrations be reduced before unclamping to limit hypotension. We prefer maintenance of stable balanced anaesthesia and manipulation of haemodynamic parameters using the techniques described.

Increasing alveolar ventilation is a strategy that will induce partial "respiratory compensation" for the metabolic acidosis that is related to the period and height of the aortic cross-clamp. In addition, the administration of sodium bicarbonate may be considered before unclamping, particularly if a high cross-clamp has been applied. Correction of metabolic acidosis does not reduce the degree of arterial hypotension post aortic unclamping.

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