Pulsatile Flow During Cardiopulmonary Bypass: Is it Beneficial?

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Abstract

(J. Extra-Corpor. Technol. 20[1]: p. 24-29, 60 references, Spring 1988) **Pulsatile perfusion has been a topic of great controversy for many years. This paper reviews historical aspects of pulsatile perfusion, as well as current and conceptual aspects of pulsatile perfusion. The positive and negative points of pulsatile perfusion are discussed so the reader may draw conclusions in an informed way. Although organ preservation and metabolic functions point towards pulsatile perfusion positively, the current knowledge demonstrates that further research would be beneficial and also notes that pulsatile perfusion is beneficial in select cases.**

Introduction

The controversy over pulsatile and nonpulsatile perfusion during cardiopulmonary bypass continues today without great prospects for resolution. This review will attempt to bring out aspects of pulsatile perfusion that may be beneficial in certain cases. The body of literature is relevant to the topic and will be followed by a short conclusion.

I: The History of Pulsatile Perfusion

The debate concerning the importance of the pulses started with the conflicting views of Appocrates, Aristotle, and Galen.[1] Two hundred years after the discovery by Harvey[2] of the relationship of the pulses to the circulation, Hamel[3] reported one of the first laboratory studies of the pulses. The introduction of clinical cardiopulmonary bypass (CPB) stimulated the initial laboratory studies of pulsatile and nonpulsatile perfusion by Wesolowski and associates.[4,5] These studies showed no pronounced difference between the two forms of perfusion.

Along with the clinical successes quickly accumulated with the simple and efficient nonpulsatile roller pump, the laboratory work of Wesolowski's group made nonpulsatile perfusion the "gold standard" for CPB. After the appearance of these studies, the controversy abated and pulsatile perfusion was relegated to physiology laboratories.[6] With the advent of ventricular assist devices (VAD), intra-aortic balloon pumping (IABP) and new perfusion technology, nonpulsatile CPB is being seriously challenged as the clinical standard.[7]

II: Physiological Hemodynamics

The study of the blood flow as a pulsatile phenomenon is scarcely new, but it has gained new impetus from three developments: 1) The commercial production of reliable flowmeters, 2) the formulation of theories appropriate to oscillatory flow in blood vessels,[7] 3) and the increasing availability of digital computers.[8] Simple inspection of the contour of pressure and flow waves is instructive, but quantitative analysis yields additional information. There are two reasons in particular for believing that such an analysis will prove useful in clinical medicine. One is that normal function in at least some organs seems to depend on the size of the pressure and flow pulsations that reach the microcirculation. The other is that abnormal transmission of these pulse waves from the heart out to the periphery has been found in some pathologic states. Since these facts imply that disturbances of pulsatile flow may account for some manifestations of disease, they are worth considering in more detail before going on to ways of analyzing and interpreting pulsations.[8] Experiments in which constant flow has been substituted for the normal pulsatile perfusion of the kidneys over a long period of time have shown a reduction in urine volume. Similar

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experiments on the circulation to the brain have been accompanied by a decrease in cerebral oxygen consumption. In addition, experience with surgical procedures that require prolonged CPB suggest that the vascular bed itself functions best if exposed to pulsatile pressure. If the arterial flow provided by a mechanical pump is nonpulsatile, or nearly so, there is often a gradual rise in peripheral resistance and mortality.[8]

The mechanism of these changes, if in fact they depend on the presence or absence of pulsation rather than some factor not yet identified, must reside in the microcirculation.[8] Transcapillary exchange is controlled in part by intracapillary pressure, including the magnitude of pulsation as well as mean pressure. These pulsations amount to several millimeters of mercury and can be increased or decreased by changes in the transmission properties of the arterial tree. Whether a capillary is open, closed, or partially collapsed also depends on transmural pressure, and here, too, the pulsations of pressure presumably have an influence. This effect has been demonstrated in the pulmonary circulation, and probably occurs everywhere, so that the concept of "critical closing pressure" should include pulsatile as well as mean pressure, and perhaps pulse frequency.

Arterioles and venules are normally subjected to pulsatile pressures that may, because of the active response of vascular smooth muscle to stretching, influence local vascular tone. In addition to these somewhat speculative possibilities, there is the well-documented fact that arterial pulsations provide much of the driving force for lymphatic flow.[8] Wilkins and associates suggested in 1962 that the physical properties of pulsatile flow better maintained microcirculation, lymphatic flow, and aerobic metabolism. Nonpulsatile flow was said to produce stagnation of the microcirculation thereby opening arteriovenous shunts and producing poor lymph flow and edema, culminating in a shift toward anaerobic metabolism.[9]

Through direct observation of the cerbral and conjunctival microcirculation, Matsumoto and colleagues noted vasodilation of venules, sludging in the microcirculation, and edema formation during nonpulsatile flow. These changes were not seen with pulsatile flow.[10] Flow in normal capillaries has been shown to be markedly pulsatile.[11]

Indirect evidence indicates that more edema results from nonpulsatile bypass. Higher fluid requirements, larger transfusion volumes, and increased generalized edema have been noted during nonpulsatile CPB.[6] Taylor et al. reported no significant differences in blood counts and plasma free hemoglobin between pulsatile and nonpulsatile CPB, suggesting that pulsatile CPB is as safe as nonpulsatile CPB from a standpoint of hematological dynamics.[12]

Dunn et al. noted that the most consistent difference between the pulsatile and nonpulsatile groups was the lower systemic vascular resistance (SVR) during CPB.[13] Pulseless blood flow alters the pattern of carotid and aortic baroreceptor impulses which can elevate SVR, increase lactate acid production, and decrease oxygen consumption,[14] whereas pulsatile perfusion significantly decreases SVR.[12] The increased clinical awareness of excessive vasoconstriction after CPB procedures has been reflected in studies concerned with the pathophysiology and treatment of the elevation in SVR. Vasoconstriction is a potentially hazardous situation in the early post-bypass period, since left ventricular work is increased and sub-endocardial perfusion may be significantly decreased.[15-17]

Therefore, the use of pulsatile perfusion during CPB offers the possibility, of preventing or minimizing the potentially harmful elevation in SVR during the post-bypass period.[12]

III Metabolic Components

A. Hormonal Effects

Hormonal responses may be responsible for several of the reported difference between pulsatile and nonpulsatile CPB. Hickey et al. reported on a number of studies demonstrating levels of epinephrine and norepinephrine were significantly higher in patients who received nonpulsatile versus pulsatile perfusion.[6]

In studies of plasma renin activity, Landymore and colleagues found significantly lower activity after bypass in patients having pulsatile CPB. Philbin and associates did not observe a significant difference between the two groups in renin activity after bypass. However these patients received propranolol hydrochloride preoperatively, whereas in the patients of Landymore and co-workers, propranolol was discontinued twenty-four hours preoperatively. Levels of angiotensin II, an end product of renin, were found to be significantly lower in separate studies by Watkins and Taylor.[18,19] Thus, the reported increases in levels of catecholeamines, renin, and angiotension II during and after nonpulsatile CPB, have been attenuated by pulsatile bypass in some studies. These same studies that demonstrated lower hormonal levels with pulsatile CPB, demonstrated lower SVR during bypass and decreased hypertension after bypass.

Plasma levels of vasopressin have been shown to increase during nonpulsatile CPB.[20-22] This increase in vasopressin was diminished during pulsatile CPB, as reported by Philbin and associates.[23,24] Increased levels of vasopressin seen during nonpulsatile CPB contribute to decreased urine output intraoperatively and may

contribute to elevated SVR and hypertension postoperatively.[6] Taylor and associates, in two separate studies showed that levels of thyroid-stimulating hormone (TSH), a hormone secreted by the anterior pituitary gland and cortisol, a steroid secreted by the adrenal glands, are better preserved during pulsatile CPB than during nonpulsatile CPB.[25,26] This along with previously discussed hormonal changes during CPB, suggests that pulsatile CPB is superior to nonpulsatile CPB in preserving metabolism and organ function.

B. Organ Preservation

1. Cerebral

The effects of pulsatile and nonpulsatile CPB have not been studied extensively. Halley et al. studied brain metabolism during CPB and showed decreased cerebral oxygen consumption but were unable to document a corresponding increase in venous lactate levels.[27] Geha and associates studied lactate and pyruvate levels, in both the cerebrospinal fluid and blood, in dogs with pulsatile CPB. Serum levels of lactate were elevated during nonpulsatile CPB, but cerebrospinal fluid levels showed no increase in lactate. They concluded that pulsatile CPB offered no great advantage over nonpulsatile CPB.[28]

Sanderson and Wright found diffuse nerve cell changes after two and three hour nonpulsatile perfusions. These changes included acute swelling in the cerebellar Purkinje cells and ischemic changes in several regions of the brain, most frequently the cerebral cortex and cerebellar Purkinje cells.[29,30] Although these studies do show some positive effects of pulsatile perfusion on the brain, these studies are isolated and over 10 years old. With evolving perfusion technology and materials, i.e., oxygenators, arterial filtration, and pumps, these areas need more investigation to draw firm conclusions.

2. Myocardium

Unlike the rest of the organs of the body, the heart has the ability to deliver pulsatile flow to itself, regardless of the method by which the aorta is perfused. There are four ways to perfuse the heart during CPB: pulsatile flow to a beating heart, nonpulsatile flow to a beating heart, pulsatile flow to a filbrillating heart, and nonpulsatile flow to a fibrillating heart.[31]

While the importance of pulsatile perfusion on peripheral organ function has been demonstrated, less is known about the relationship between pulsatile flow and myocardial perfusion. During CPB with linear perfusion, blood flow through the coronary arteries in the beating heart is phasic by virtue of rhythmic cardiac contraction and the associated rhythmic variation in intramural pressure. However during elective ventricular fibrillation, while on total CPB, linear perfusion results in linear coronary flow.[32] In the presence of critical coronary stenosis, ventricular fibrillation with linear perfusion produces a regional inequality and imbalance between oxygen supply and demand, resulting in regional myocardial ischemia.[32] Ventricular fibrillation also induces a gradient in intramyocardial tissue pressure; higher in the subendocardium than in the subepicardium.[33]

With adequate coronary perfusion pressure and unobstructed coronaries, the tissue pressure should not cause significant limitation of coronary flow, and in fact, coronary flow increases in subendocardial layers to meet the higher oxygen demand of fibrillation.[34] In the presence of critical coronary stenosis, perfusion pressure distal to the coronary stenosis is 30-40 mmHg lower than aortic root pressure.[35] At this lower pressure in the distal coronary artery, perfusion pressure may approach the intramyocardial pressure. If the net coronary pressure (intracoronary pressure-tissue pressure) falls below a "critical closing pressure" of the capillaries, tissue perfusion would be reduced. By this mechanism of capillary closure, a cycle could develop by which local ischemia leads to a change in vascular permeability and tissue edema, futher compromising local perfusion and leading to a futher increase in the degree of ischemia. The higher systolic pressure during pulsatile perfusion might act to keep capillaries open even if the net mean perfusion pressure is below the critical capillary closing pressure.[32]

Milnor states that transcapillary exchange is controlled partially by intracapillary pressure, and it may be influenced by the magnitude and rate of pulsations as well as the mean pressure. It is pointed out that pulse pressure in the capillaries normally amounts to several millimeters of mercury and that this pulsation of pressure, in addition to mean pressure, might effect whether a capillary is open, closed, or partially closed. In addition, the smooth muscles of arterioles and venules are normally subjected to pulsatile pressures, and absence of such pulsation may affect vascular tone. Pulsatile perfusion also augments tissue lymph flow and thereby might tend to reduce edema. Thus, pulsatile perfusion may prevent further increases in intramyocardial tissue pressure by interrupting the cycle of capillary closure leading to more capillary closure.[8]

It would seem apparent that pulsatile perfusion during CPB would better preserve the myocardium. In a critical review of numerous studies, Hickey et al. noted that there were an equal number of studies showing no difference in myocardial function as there are studies showing a difference postoperatively between pulsatile and nonpulsatile CPB.[6]

During cardioplegic arrest, the advantages to the

heart of pulsatile perfusion are limited to the pre-arrest period of bypass and to the reperfusion period. Reperfusion injury after careful cardioplegic arrest (but not after normothermic ischemic arrest) may be ameliorated by pulsatile perfusion, perhaps because of its beneficial effect on the myocardial oxygen supply to demand ratio, and on coronary microcirculation.[36]

There is an injury unique to hypothermic hyperkalemic cardioplegic arrest that has been documented by various investigators.[36-42] Myocardial biopsy specimens obtained at the time of open hear operation showed ultrastructural abnormalities and decreases in high energy nucleotide levels, specifically adenosine triphosphate (ATP) thirty minutes after the restoration of coronary flow that were not evident prior to aortic unclamping.[43-47] Silverman et al. demonstrated in this same study that ATP stores were decreases by 23% in patients receiving nonpulsatile verses pulsatile perfusion.[36]

Reperfusion injury following cardioplegic arrest may be a result of minimal injury accrued during ischemia and augmented by the increase in energy requirements associated with the return of electromechanical activity. The beneficial effects of pulsatile perfusion in augmenting collateral and subendocardial blood flow and improving the ratio of myocardial oxygen supply to demand have been clearly shown in ischemic preparations not involving CPB and have been extrapolated to the situation of myocardial ischemia during CPB.[48-50]

Pulsed flow improves coronary perfusion pressure both prior to the establishment of a stable supraventricular rhythm and when sychronized, with the electrocardiogram after defibillation. Moreover, pulsed flow maintains patency of the microvasculature by overcoming the compressive forces of increased interstitial pressure, which is particularly important for subendocardial perfusion.[36]

The hemodynamic effects off pulsatile flow must be sufficient to augment coronary flow or diminish myocardial work to offset the heart's diminished ability to utilize oxidative metabolism for nucleotide synthesis.[51] Although the mechanism whereby pulsatile reperfusion prevents the metabolic derangements noted after cardioplegic arrest has not been elucidated, its continued clinical application appears warranted in selected patients. Nevertheless, it is no substitute for adequate intraoperative myocardial protection.[52]

3. Renal

The earliest studies of the arterial pulse were made in the isolated perfused kidney. Gesell postulated that pressure changes in the form of "vascular shocks" promote better flow of lymph in the microcirculation and greater gas exchange in the capillaries.[53] Corcoran and others showed that release of renin is stimulated by decreased pulse pressure rather than reduced mean arterial pressure.[54]

More recent experiments indicate uniform advantages of pulsatile blood flow. Nakayama et al. noticed a 10% greater renal venous return with pulsatile blood flow. They also noted that kidneys, perfused with nonpulsatile CPB, were found to have microscopic ischemia and that renal blood pooling tended to be greater in these groups. These changes were not found in the pulsatile groups.[55]

Many et al. noted that reducing pulse pressure to the kidney resulted in decreased urine output and sodium excretion. These changes were observed while mean arterial pressure, mean renal blood flow, glomerular filtration, and renal plasma flow remained unchanged. Based on histological studies that showed larger tubular lumens in depulsated kidneys, Many's group proposed that the apparent decrease in sodium excretion and urine output might be explained by stagnation of the filtrate in the tubules, thereby increasing transit time and sodium reabsorption, and secondarily affecting water absorption.[56]

Paquet showed in the isolated pig kidney that nonpulsatile flow resulted in acidosis, decreased oxygen consumption, impaired renal function, and increased renal vascular resistance.[57] Perhaps one of the most important roles of the pulse has been shown in renal homograft preservation. Belzer et al. found that pulsatile flow produces better cortical perfusion in the preserved kidney, which appears to result in more rapid restoration of renal function after implantation.[58]

Renal studies suggest that pulsatile perfusion better preserves renal function, maintains more normal renal metabolism, reduces renal renin release, better preserves outer cortical flow, and prevents ischemic changes, especially during longer periods of perfusion.[6]

4. Pancreatic

Nonpulsatile CPB has been associated with increases in serum amylase and amylase-creatinine clearance ratios, postoperatively. Hickey et al. reports many documented cases of pancreatitis following nonpulsatile CPB.[6] A 10% incidence of unexplained pancreatitis at postmortem examination after cardiac operations was reported by Feiner.[59]

Evidence from this report and from that of Warshaw and O'Hara, suggest that ischemia may be an important factor in pancreatitis after bypass.[60] Two recent clinical studies have shown that abnormalities in serum amylase and amylase-creatinine levels are significantly higher after nonpulsatile CPB than after pulsatile CPB. The

presumed defect in perfusion is in the microcirculation. It is only speculation, however that the clinical pancreatitis after nonpulsatile CPB is related to the nonpulsatile nature of bypass rather than to low flow or hypotension during and after bypass.[6]

Conclusion

Pulsatile perfusion is a physiologic phenomena made up of numerous physical properties. Pulse frequency and vascular impedance have a major effect on the form pulsatile flow assumes regardless of the perfusion source.

Failure to appreciate the basic physical nature of pulsatile flow has led to a controversy in which perfusion has been dichotomized into "pulsatile" and "nonpulsatile" flows. Studies differentiating the two types of perfusion only perpetuate this false dichotomy that pulsatile perfusion is a singular, straight-forward phenomenon like nonpulsatile perfusion. Various studies suggest that pulsatile CPB better preserves normal metabolism, increases physiologic oxygen consumption, and yields better preservation of vital organs than nonpulsatile CPB. There are studies that suggest there is no major difference between the two forms of perfusion. This would warrant continued research in this area. Even though the literature has mixed views on this issue, pulsatile CPB could be very beneficial in patients with renal disease, peripheral vascular insufficiency, and those with possible reperfusion problems such as left ventricular hypertrophy.

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