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Pro and Con

Con: Pulsatile Flow During Cardiopulmonary Bypass

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THE DEBATE ON THE efficacy of the pulsatile flow (PF) compared to the non-PF is fascinating. This is due to the growing use of cardiocirculatory assistance techniques, extracorporeal membrane oxygenation (ECMO), and extracorporeal circulation during cardiac surgery. The authors tried to evaluate the potential limits of the effectiveness of PF, considering the evidence coming from the literature.

More than a million cardiac surgical procedures are performed each year worldwide. Many of these are done with the help of cardiopulmonary bypass (CPB).[1] Cardiopulmonary bypass has been the subject of many studies and insights, as well as continuous improvements of its materials to make it more and more biocompatible.[1,2]

Much also has been studied regarding the nature of the flow, with particular attention to organ protection as the best indicator of the effectiveness of the type of flow (pulsatile or continuous) used. Having a PF that would mimic the physiologic flow is undoubtedly a desirable condition. This is because it represents a crucial point for ensuring organ perfusion during CPB and ECMO.[2]

Few topics have been studied as thoroughly as flow during CPB. The data available to date are minimal regarding the effects of 2 different blood flows, pulsatile and continuous, on microcirculation.[2]

Many authors have underlined that the PF is superior to the continuous flow during CPB. Despite that, to date, the technologic development of pulsatile pumps is minimal due to technical difficulties and the lack of interest by companies in developing pulsatile pump systems. The reason is that there are still little data in the literature, and the existing ones need solid confirmation. The attention to this aspect arises precisely from the desire of the researchers to mimic the pulsed arterial flow as it occurs physiologically.[1,2]

It has been demonstrated that, in experimental conditions, non-PF leads to lower endothelial shear stress, causing an increase in vascular resistance.[3] Considering the opposite, by increasing nitric oxide production, the PF would preserve perfusion at any microcirculatory site.[4]

Pulsatile flow production can occur using PF generators within the CPB circuit or external systems, such as the intraaortic balloon pump (IABP). The components of PF comprise the following: (1) the non-pulsatile component of stroke volume, (2) the percentage of each cycle that is spent in systole, and (3) the frequency of pulsatility (number of cycles per minute).[1] The evidence shows that a better PF can be generated during low blood flow support with extracorporeal circulatory systems.[2] However, this setting cannot be applied in patients with severe decompensation of the native heart function, as they require increases in cycles and pump accelerations to maintain adequate blood flow and oxygen delivery to tissues. Unfortunately, this can increase hemolysis.[5] For this reason, attempts have been made to synchronize some pulsatile pumps with electrocardiographic tracing. Of course, this technique loses its effectiveness when the heart stops beating due to cardioplegia.

The authors analyze below the evidence about the effects of PF on microcirculation and subsequent organ perfusion improvement and protection. Also, they address what the evidence offers about the potential benefits, if any, of using PF.

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The Microcirculation

The microcirculation certainly represents one of the most studied areas for evaluating the efficacy of PF. Studies investigating sublingual microvascular perfusion with orthogonal polarization spectral or sidestream dark field imaging did not show significant differences in the number of normally perfused vessels between patients undergoing PF and non-PF.[6-10] Unfortunately, considering the effects of PF on microcirculation, the evidence in the literature is weak. The reason is that the studies in this field were very heterogeneous because they were conducted on different patient populations; in addition, some findings came from animal models, and different types of devices were applied during CPB or ECMO to create pulsatility (ie, IABP or other pulsed pumps). These drawbacks make it difficult to highlight a real benefit of the PF on the microcirculation.[11]

Finally, the kinetics of many biomarkers and interleukins, as subclinical surrogate indicators of microcirculatory derangement, have been studied without an orderly and univocal approach. Thus, in analyzing the individual studies about the effects of PF versus non-PF on microcirculatory function, no meaningful differences were found in animals or humans.[9,10,12]

As PF can be generated either by ECMO components or IABP, and before proceeding with the description of the effects of PF on the main organs and systems, it is essential to clarify that pulsatile components of flow during ECMO (or CPB) are flow improvement strategies still under investigation and with little or theoretical clinical applications. The pulsatile component generated by IABP is mainly a left ventricular unloading system that reduces the left ventricular afterload (during deflation) and improves coronary perfusion pressure (during inflation).

The Kidneys

The studies that have analyzed the efficacy of PF on renal function to date are few.[13,14] Only 1 has shown an increase in urine output and an improvement in creatinine clearance.[15] PF did not reduce the incidence of acute kidney injury and the risk reduction of developing renal failure. However, the clinical evidence of kidney protection rises when IABP generates the PF during CPB.[16-18] The intra-aortic balloon pump cannot be considered a device that produces PF in the strict sense. In addition, a large meta-analysis did not demonstrate beneficial aspects in the pulsed group with IAPB compared with the nonpulsed group.[19]

The Lungs

Considering the lungs, even in this case, the evidence came from studies in which IABP was used to generate PF. However, the results are encouraging in terms of reduction of the duration of mechanical ventilation, better PaO_2/fraction of inspired oxygen ratio, improved pulmonary compliance, and reduction of the need for postoperative noninvasive ventilation in the pulsatile group compared with a nonpulsatile group.[20,21] Notably, if the PF is generated using roller or centrifugal pumps equipped with PF-generating devices, the clinical evidence of lung protection tends to be less intense.[22,23]

The Splanchnic District

The splanchnic area is generally one of the most challenging sites to study. Moreover, it is also the one where hypoperfusion could generate a pivotal injury considering the number of organs it includes and the critical role it plays in many pathophysiologic processes. Again, the PF generated by IABP did not show significantly better results than the non-PF flow.[24-27] Only 1 study demonstrated that the PF improved the perfusion evaluated at the level of the gastric mucosa.[13]

The Brain

The attention in this area is more focused on evaluating cognitive dysfunctions and the onset of cerebrovascular injuries.[28,29] Some studies have demonstrated improved cognitive function in patients undergoing PF; however, no difference was shown in the incidence of major cerebrovascular events (eg, stroke, coma) between the pulsed and nonpulsed groups.[30] Once again, the PF was generated by IABP.[28,30] In an interesting study, Veraar et al. hypothesized that the loss of pulsatile brain perfusion would be implicated in neurologic complications related to changes in brain CO_2 reactivity. The authors studied 32 patients undergoing elective cardiac surgery in this prospective, single-center, case-controlled trial. They found that nonpulsatile perfusion was associated with enhanced cerebrovascular CO_2 reactivity, which resulted in a more significant relative decrease of cerebral blood flow (CBF) during hypocapnia.[29]

The PF reduced the production of significant cytokines without evident perfusion effects. This also applies to CBF, for which there is no evidence that modulating the concentration of proinflammatory and anti-inflammatory major cytokines could affect the blood-brain barrier integrity, modify CBF, or alter brain function.

The Cardiovascular System

The effects of PF generated by IABP on the cardiovascular system are much stronger than those on other anatomic sites. However, these results should be interpreted in light of the direct beneficial effects of IABP on the cardiovascular system but not on the PF that this device generates during CPB.[8,20] No significant differences were observed in troponin I or creatine kinase levels between pulsed and non-PF groups when the PF was produced through roller or centrifugal pumps equipped with PF-generating devices.[20,21,31] The evidence about the efficacy of the PF generated during CPB is still poorly understood and arises, as previously said, from heterogeneous studies.[6,7,32]

The situation is different when the attention is focused on the PF during ECMO.[33,34] The continuous retrograde ECMO impairs the pulsatility of blood flow created by the native cardiac ejection, and this condition may affect organ perfusion and tissue metabolism.[33] Moreover, the beneficial effects of ECMO must be balanced with several risks it could determine,

such as coagulation disorders, systemic inflammatory response, increase in systemic vascular resistances, and intravascular sludging. All these factors may impact microcirculation negatively.[33,34]

One of the most recent papers (published by Li et al. in 2022) concluded that PF during ECMO enhanced microcirculatory perfusion and stabilized endothelial integrity, which could be considered a protective factor on microcirculation as it could attenuate endothelial inflammation. However, how PF or non-PF blood flow impacts this aspect is not well-documented, as the conclusions of many papers are obtained from animal studies and never replicated in humans.[33,34]

Conclusions

Although there is some evidence that PF usage during CPB may enhance lung and kidney function, the impact on clinical outcomes seems minimal. However, it should be remembered that PF is only recommended for cardiac patients at high risk of pulmonary and renal complications.[32]

Many studies agree that there is no difference in survival and intensive care unit length of stay in the PF group compared with the non-PF group, and any conclusion should be considered speculative.[11,32] Continuous-flow ventricular assist devices have become pulsatile over the past 10 years for long-term and short-term circulatory support. Also, much of the data supporting PF come from studies in which an IABP was used to create pulsatility. The results of these trials cannot be extrapolated to the general cardiac surgical population, and the routine use of PF during CPB cannot be advised. The major perplexities about the use of PF arise from the following considerations: (1) the real possibility of replicating a PF proper, (2) the absence of significant evidence about the actual benefits, and (3) the benefits of PF are well documented in studies where IABP generates PF during CPB or ECMO, which is not strictly to be considered as proper PF.

Whether the routine use of PF during CPB or ECMO would improve clinical practice and patient outcomes is still unknown.

Declaration of Competing Interest

None.

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