Pulsatil Akýmlý Kardiyopulmoner Bypassýn Pediyatrik ve Yetiþkin Açýk-Kalp Hastalarýnda Kullanma Prensipleri

PRINCIPLES AND PRACTICES OF PULSATILE PERFUSION IN PEDIATRIC AND ADULT OPEN-HEART SURGERY

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Özet

Son 10 yýlda pediyatrik ve eriþkin kardiyopulmoner bypass (KPB) prosedürlerine baðlý ölümler anlamlý derecede azalmýþtýr. Ancak morbidite halen ciddi klinik bir problem olmaya devam etmektedir. Özellikle de yüksek riskli hastalar KPB sonrasý serebral, renal ve miyokardiyal disfonksiyona yatkýndýrlar. Birçok araþtýrma KPB'nin bu yüksek riskli haztalardaki etkilerini azaltmak için yapýlmaktadýr. Perfüzyon tipinin (pulsatil veya nonpulsatil) vital organlarýn geri düzelmesinde direkt etkisi vardýr. Modern perfüzyon pompalarý pulsatil ve nonpulsatil akým seçenekleri sunmaktadýrlar. Pulsatil akýmýn yararlarýnýn ortaya konmasýna karþýn, birçok merkez hala non-pulsatil akýmý tercih etmektedir. Pulsatil akýmýn kullanýlmama nedenleri bu yazýda tartýþýlacaktýr. Ayrýca pulsatil akýmýn klinik kullanýmý adým adým açýklanacak ve gelecek araþtýrmalar anlatýlacaktýr. Özellikle de, çeþitli pulsatil ve non-pulsatil pompalar enerji eþittir basýnç formülüne göre basýnç-akým dalgalarý ve toplam hemodinamik enerji düzeyleri açýsýndan karþýlaþtýrýlacaktýr.

Anahtar kelimeler: Pulsatil akým, devamlý akým, kardiyopulmoner bypass

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Summary

During the past decade, the mortality rates following pediatric and adult cardiopulmonary bypass (CPB) procedures have been significantly reduced. But, the morbidity is still a significant clinical problem. Particularly, high-risk cardiac patients suffer cerebral, renal, and myocardial dysfunction after CPB. Several investigations now focus on research in minimizing the adverse effects of CPB in high-risk patients. The mode of perfusion (pulsatile or non-pulsatile) has a direct impact on vital organ recovery. Modern perfusion pumps provide the option of pulsatile and non-pulsatile flow. Despite the growing evidence for the possible benefits of pulsatile flow, the majority of institutions still choose to use non-pulsatile flow. The reasons for not using pulsatile flow relate to controversies and lack of sufficient evidence. These will be addressed in this editorial. In addition, step-by-step guidelines for the use of pulsatile flow in clinical patients for future investigations will be described. Particularly, the quantification of pressure-flow waveforms in terms of energy equivalent pressure and total hemodynamic energy levels, different types of pulsatile and non-pulsatile pumps, and the pressure drops seen in membrane oxygenators and aortic cannulas will be included.

Keywords: Pulsatile flow, non-pulsatile flow, cardiopulmonary bypass

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Introduction

Although the benefits of pulsatile perfusion during pediatric and adult cardiopulmonary bypass (CPB) procedures are clearly documented in the literature, the controversy still continues [1-20]. The following are the three main reasons for this long-standing controversy. 1) Lack of precise quantification of arterial pressure and pump flow waveforms: To date, we do not have a common or universal definition of pulsatile flow [20-22]. Without a definition or a precise quantification, it is impossible to make direct and meaningful comparisons of different perfusion modes [1,2]. 2) Poor choice of pulsatile pumps and disposables: Each component of the circuit must be selected based on its previous performance in different perfusion modes because not only the pulsatile pump, but also the membrane oxygenator and the aortic cannula each have a direct impact on the quality of pulsatility [23-25]. Unfortunately, most of the investigators today select circuit components without any scientific justification. 3) Limitations of experimental designs: Several investigators in the past used pulsatile flow for only a few minutes, then expected to see significant improvement in cerebral function [26,27]. In order to see the benefits of pulsatile flow, it should be used continuously during CPB. In addition, patient selection is another important factor for meaningful comparisons between

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perfusion modes. Vital organ injury does not happen in every single case after CPB. If there is no vital organ injury, then it is impossible to show any benefits of pulsatile perfusion. A detailed list of other limitations was discussed in our earlier publication [2].

Definition of Pulsatile and Non-Pulsatile Flow

Most of the investigators today believe that if the pulse pressure is greater than 15 mmHg, then the pump flow is considered as a pulsatile flow [28]. If the pulse pressure is less than 15 mmHg, then the flow is non-pulsatile. In the past 50 years only a few investigators have tried to quantify pulsatile and non-pulsatile flow in terms of hemodynamic energy in order to perform comparison [20-22,28-32]. Quantification of pulsatility in terms of pulse pressure is inadequate because the generation of pulsatile flow depends on an energy gradient rather than a pressure gradient [29]. In addition to the pulse pressure, pump flow rate and arterial pressure must be included in quantification of different perfusion modes. To date, Shepard's Energy equivalent pressure (EEP) and total hemodynamic energy formulas are the best tools for a pricise quantification of pressure-flow waveforms [29].

Energy Equivalent Pressure

The EEP formula is based on the ratio between the area beneath the hemodynamic power curve (∂ fpdt) and the area beneath the pump flow curve (∂ fdt) during each pulse cycle:

EEP = (∂ fpdt) / (∂ fdt)

where *f* is the pump flow rate, *p* is the arterial pressure (mmHg), and *dt* is the change in time at the end of flow and pressure cycles. The unit of the EEP is mmHg.

Total Hemodynamic Energy

Using Shepard's total hemodynamic energy formula, ∂ [(ergs/cu cm) = (1.332 ∂ pfdt) / (∂ fdt)] the constant 1.332 changes pressure from units of millimeters of mercury to units of dynes per square centimeters [29].

The following are examples of EEP and total hemodynamic energy levels seen during pulsatile and non-pulsatile perfusion: When the physiologic pulsatile pump is used in a neonatal piglet model with a pump flow rate of 150ml/kg/min, a mean arterial pressure (MAP) of 40 mmHg, and an extracorporeal circuit pressure (ECCP) of 70 mmHg, then the EEP is 101.5 mmHg [32]. 101.5 mmHg is 45% higher than 70 mmHg [32]. The difference between the EEP and the ECCP is 31.5 mmHg which is the extra energy generated by the physiologic pulsatile pump. In order to calculate the total hemodynamic energy, we multiply 31.5 mmHg by 1322 [(dynes/sq cm) / (mmHg)]. This results in 41.958 ergs/cu cm.

When the pulsatile roller pump is used with the identical ECCP, MAP and pump flow rate, the EEP is 80 mmHg. 80 mmHg is 14.5% higher than 70 mmHg [32]. The difference between the EEP and ECCP is 10 mmHg. This 10 mmHg represents (10 x 1.332) 13.320 ergs/cu cm.

When the non-pulsatile roller pump is used with the identical pressures and pump flow rates, the EEP is 71.3 mmHg. 71.3 mmHg is 1.9% higher than 70 mmHg [32]. The difference between the EEP and the ECCP is only 1.3 mmHg. 1.3 mmHg represents (1.3 x 1.332) 1,732 ergs/cu cm.

Therefore, the difference in total hemodynamic energy between the physiologic pulsatile pump and the pulsatile roller pump is 28.638 ergs/cu cm (41.958-13.320 = 28.638), between the physiologic pulsatile pump and the non-pulsatile roller pump 40.226 ergs/cu cm (41.958-1.732 = 40.226), and between the pulsatile roller pump and the non-pulsatile roller pump 11.588 ergs/cu cm (13.320-1732 = 11.588). I truly believe that these significant extra hemodynamic energy levels generated by the physiologic pulsatile pump or a pulsatile roller pump maintain more physiological capillary perfusion, less systemic inflammation, better vital organ recovery, and improved clinical outcomes [1-20,30,33]

Guidelines for use of pulsatile perfusion in clinical research

Step 1. Literature review

Prior to in-vitro or in-vivo experiments, a current literature review is a must. As of March 6, 2004, a Medline search with "Pulsatile CPB" key words results in 131 publications. Investigators who have an interest in pulsatile perfusion must read at least 40 to 50 recent articles since the 1990's in order to identify suitable patients, pulsatile pumps, membrane oxygenators, and aortic cannulas.

Step 2. In-Vitro Evaluation

Once the components of the circuit are chosen, an in-vitro test is the second step. Perfusionists must configure a circuit with a pseudo patient, and adjust all physiological parameters for this test. We have already published a design for a pediatric CPB patient for other investigators [24]. This particular circuit can be easily adapted in to an adult loop by changing the tubing size, installing a larger membrane oxygenator, and adjusting the arterial pressure and pump flow rates.

Pulsatile pumps: All FDA approved pulsatile pumps in the United States generate only diminished pulsatility, not physiological pulsatility. We have already documented that the pulsatile roller pump with a diminished pulsatile flow is significantly better than non-pulsatile perfusion in terms of vital organ recovery during and after CPB [18]. Some of the pulsatile pumps do not generate any pulsatility at all compared to non-pulsatile perfusion [34]. Therefore, each investigator must determine the degree of pulsatility prior to using it in a clinical or experimental set-up. Arterial pressure and pump flow waveforms must be recorded.

Pulsatile pump rate: When the pulsatility is turned on, the pump rate must be pre-set to 60 to 80 bpm for adults and 80 to 120 bpm for pediatric patients. For neonates and infants, pulsatile pump rate can be increased up to 150 bpm.

Base flow: In order to generate pulsatile flow, the roller pump head starts and stops. If the pump head stops completely, then starts again 120 times per minute, it may create microemboli. In order to avoid microemboli, base flow should be set no lower than 10%. For first time users, I highly recommend setting the base flow to 30%. Base flow means continuous or non-pulsatile perfusion. With a base flow of 30%, we have only 70% pulsatile flow and 30% non-pulsatile flow, but the roller head does not stop at all during pulsatile perfusion.

Membrane oxygenators: The pressure drops of the membranes must be recorded and compared at different pump flow rates with pulsatile and non-pulsatile perfusion. If the pressure drop is lower, that means that particular oxygenator has lower resistance to the blood flow, and it causes less blood trauma and systemic inflammation during CPB [17,24,35]. There is no question that hollow-fiber membrane oxygenators are superior

to other types of membrane oxygenators. But the structure of the hollow-fibers has a direct impact on the quality of the pulsatility. Therefore, all different brands of hollow-fiber membrane oxygenators must be compared in terms of pressure drops and arterial pressure and pump flow waveforms.

Aortic cannula: The cannula size used has a significant impact on the quality of the arterial pressure waveforms. The larger the cannula tip, the better the pulsatility [25]. Therefore, the ability to achieve adequate pulsatility in adult patients is not an issue. Generating sufficient pulsatility in neonates and infants with an 8 or a 10 Fr aortic cannula can be difficult. We have already documented that it is possible to produce adequate pulsatility with the different geometries of the aortic cannulas [25]. The 8 or 10 Fr aortic cannula with a shorter tip allows better pulsatility [25].

Arterial filters: Arterial filters do not have any adverse effects on pulsatile perfusion.

Step 3. In-Vivo Evaluation

After the selection of all the components of the circuit, a few animal experiments are highly recommended. At the end of each experiment, evaluation of vital organs in terms of immunohistopathology will give significant details which are not possible after clinical studies. In addition, it is extremely important to give the perfusionists the opportunity to pump a few animal cases before any clinical trials.

Step 4. Pilot clinical study

After finalizing the selection of the pump, membrane oxygenator, aortic cannula, and completing a few animal experiments, a pilot clinical study including no more than 40 patients (20 patients in each group) should be done prior to routine use of pulsatile perfusion. Patients must be selected based on the risk stratification in each group. There should not be any significant differences in patients' weight, age, duration of CPB and cross-clamp time for meaningful comparisons. When pulsatile perfusion is used, it must start after the cross-clamp is placed, and must end before the clamp removal in all pilot experiments. During pulsatile perfusion, the pump rate must be identical for all pilot experiments. In addition, blood samples must be collected for measuring plasma free hemoglobin levels, and if possible for the measurements of complements, neutrophils, platelets, and cytokines at the initiation of CPB and at the end of CPB.

Step 5. Routine use of pulsatile perfusion

If the pilot study results are acceptable and all members of the team including surgeons, anesthesiologists, and perfusionists are comfortable with the design, then the routine use of pulsatile perfusion in clinical patients is warranted. After adequate experience has been gained with pulsatile perfusion during pilot experiments, then the pulsatility may be triggered with the EKG throughout the CPB, otherwise pulsatile flow should be used only during aortic cross-clamping.

Myths of pulsatile perfusion

Adverse effects of CPB have multi-origins. It is well-documented that high-risk pediatric and adult patients will have more significant vital organ injury compared to moderate or low risk cardiac patients [36,37]. Pulsatile perfusion only minimizes these adverse effects, it does not eliminate them. The benefit of pulsatility will be low when compared among low-risk patients. It is important to know that high-risk cardiac patients with pulsatile perfusion will benefit the most compared to other patients in lower risk stratification groups. A detailed list of myths and truths of pulsatile flow is described in our earlier publication [1].

Safety and quality of perfusion

Bubble detector, dynamic bubble trap system, and transcranial doppler

In order to reduce the number of gas or particulate emboli, a bubble detector is a necessity in both pulsatile and non-pulsatile perfusion systems. The bubble detector is placed after the oxygenator, must continuously be used during CPB, and should not be confused with an arterial filter. In addition to these safety devices, we have recently seen in the literature the successful use of a dynamic bubble trap system [38]. This particular device is placed between the arterial filter and the aortic cannula, and recent results also suggest that it may significantly reduce gaseous microemboli in adult CPB patients [38].

Transcranial Doppler is also a safety device used to detect and quantify the number of microemboli in the cerebral artery during CPB [39]. I highly recommend utilizing this particular non-invasive device because the pulsatility index can also be recorded during pulsatile and non-pulsatile perfusion for direct comparison.

Recently, investigators have developed an algorithm for improving the quality of the perfusion during adult CPB procedures [40]. This particular perfusion related protocol combines several important variables such as hematocrit, mean arterial pressure, colloid osmotic pressure, temperature, blood lactate levels, acid base homeostasis, oxygenation, coated circuitry, and pulsatile perfusion. Using the Society of Thoracic Surgeons database and their perfusion treatment algoritm, they have developed a Mortality Assessment Perfusion Score (MAPS) for each patient [40]. Another group of investigators has already designed a cardiopulmonary bypass score system to assess the quality of perfusion performance [41]. I truly believe that other pediatric and adult cardiac centers should use these existing algorithms, and develop their own system in order to improve the quality and the safety of CPB procedures [40-42].

Discussion

Pulsatile perfusion is more beneficial than conventional non-pulsatile perfusion in pediatric and adult patients if adequate pulsatility is achieved. Components of the CPB circuit must be carefully selected prior to using pulsatile flow. Arterial pressure and pump flow waveforms must be quantified in terms of energy equivalent pressure and total hemodynamic energy levels. To date, there is no credible evidence to document the adverse effects of pulsatility during pediatric or adult CPB procedures. Pro-non-pulsatile investigators can only claim that there is no difference between perfusion modes in terms of vital organ recovery while several investigators have documented significant benefits from the use of pulsatile perfusion in the literature.

Author's Note:

1. During the past ten years I have personally designed dozens of investigations on pulsatile flow in vitro and in vivo. Most of the issues discussed in this editorial are my personal experiences with both types of perfusion systems. I intentionally avoid using the names of the manufacturers for the CPB circuit components. However, if one reads the original articles cited in this paper, then he/she will see the names of the manufacturers. I declare that neither I nor any of my family members have any financial interest in the products discussed in those articles.
2. Although I wrote "For neonates and infants, the pulsatile pump rate can be increased up to 150 bpm", I strongly encourage investigators to first use pulsatile perfusion in adult CPB patients with lower pump rates. After adequate experience with pulsatile flow is achieved, then it is alright to use it in pediatric patients. Neonates and infants should be the last patient population subjected to pulsatile perfusion because of the high pulsatile pump rate of 150 bpm.

If any of the readers have any questions which are not covered in this paper, please do not hesitate to send me an e-mail aundar@psu.edu.

References

1. Ündar A. Myths and truths of pulsatile and non-pulsatile perfusion during acute and chronic cardiac support [Editorial]. Artif Organs 2004;28:439-43.
2. Ündar A. The ABCs of research on pulsatile versus nonpulsatile perfusion during cardiopulmonary bypass [Editorial]. Med Sci Monit 2002;8:21-4.
3. Orime Y, Shiono M, Hata H, et al. Cytokine and endothelial damage in pulsatile and non-pulsatile cardiopulmonary bypass. Artif Organs 1999;23:508-12.
4. Özatik MA, Tarcan O, Kale A, et al. Do S100_ protein level increases due to inflammation during cardiopulmonary bypass occur without any neurological deficit? Perfusion 2002;17:335-8.
5. Murkin JM, Martzke JS, Buchan AM, Bentley C, Wong CJ. A randomized study of the influence of perfusion technique and pH management strategy in 316 patients undergoing coronary artery bypass surgery. I. Mortality and cardiovascular morbidity. J Thorac Cardiovasc Surg 1995;110:340-8.
6. Watarida S, Mori A, Onoe M, et al. A clinical study on the effects of pulsatile cardiopulmonary bypass on the blood endotoxin levels. J Thorac Cardiovasc Surg 1994;108:620-5.
7. Taylor KM. Pulsatile perfusion. In: Taylor KM, edi. Cardiopulmonary Bypass. Baltimore: Williams & Wilkins, 1986:85-114.
8. Williams GD, Seifen AB, Lawson NW, et al. Pulsatile perfusion versus conventional high-flow non-pulsatile perfusion for rapid core cooling and rewarming of infants for circulatory arrest in cardiac operation. J Thorac Cardiovasc Surg 1979;78:667-77.
9. Yasui H, Yonenaga K, Kado H. Open-heart surgery in infants using pulsatile high-flow cardiopulmonary bypass. J Cardiovasc Surg 1989;30:661-8.
10. Fumero R, Montevecchi FM, Scuri S, Carrara B, Gamba A, Parenzan L. Clinical experience with a new pulsatile pump for infant and pediatric cardiopulmonary bypass. Int J Artif Organs 1989;12:314-20.
11. Ündar A, Masai T, Beyer EA, et al. Pediatric physiologic pulsatile pump enhances cerebral and renal blood flow during and after cardiopulmonary byass. Artif Organs 2002;26:919-3.
12. Ündar A, Masai T, Yang SQ, et al. Pulsatile perfusion improves regional myocardial blood flow during and after hypothermic cardiopulmonary bypass in a neonatal piglet model. ASAIO J 2002;48:90-5.
13. Ündar A, Masai T, Yang SQ, et al. Effects of perfusion mode on regional and global organ blood flow in a neonatal piglet model. Ann Thorac Surg 1999;68:1336-43.
14. Minami K, Dramburg W, Notohamiprodjo G, Körfer R. Effects of pulsatile perfusion on perioperative morbidity and mortality in high-risk patients. In: Minami K, Körfer R, Wada J, edi. Cardio-thoracic Surgery. What is new in Current Practice. Amsterdam:Elsevier, 1992.67-75.
15. Baba A, Dobsak P, Mochizuki S, et al. Evaluation of pulsatile and nonpulsatile flow in microvessels of the bulbar conjunctiva in the goat with an undulation pump artificial heart. Artif Organs 2003;27:875-81.
16. Ündar A, Lodge AJ, Daggett CW, Runge TM, Ungerleider RM, Calhoon JH. Design and performance of a physiologic pulsatile flow neonate-infant cardiopulmonary bypass system. ASAIO J 1996;42:580-3.
17. Ündar A. Design and performance of physiologic pulsatile flow cardiopulmonary bypass systems for neonates and infants. Ph.D. Dissertation. The University of Texas at Austin, May 1996.
18. Ündar A, Eichstaedt HC, Frazier OH, Fraser CD. Monitoring regional cerebral oxygen saturation using near-infrared spectroscopy during pulsatile hypothermic cardiopulmonary bypass in a neonatal piglet model. ASAIO Journal 2000;46:103-6.
19. Herreros J, Berjano EJ, Mas P, et al. Platelet dysfunction in cardiopulmonary bypass: An experimental comparative study between a centrifugal and a new pulsatile pump. Int J Artif Organs 2003;26:1086-94.
20. Wright G. Hemodynamic analysis could resolve the pulsatile blood flow controversy. Ann Thorac Surg 1994;58:1199-204.
21. Ündar A. Universal and precise quantification of pulsatile and non-pulsatile pressure-flow waveforms is necessary for direct and adequate comparisons among the results of different investigators [letter]. Perfusion 2003;18:135-6.
22. Ündar A. Energy equivalent pressure formula is for precise quantification of different perfusion modes [letter]. Ann Thorac Surg 2003;76:1777-8.
23. Gourlay T, Gibbons M, Taylor KM. Pulsatile flow compatibility of a group of membrane oxygenators. Perfusion 1987;2:115-26.
24. Ündar A, Koenig KM, Frazier OH, Fraser CD. Impact of membrane oxygenators on pulsatile versus nonpulsatile perfusion in a neonatal model. Perfusion 2000; 15:111-20.
25. Ündar A, Lodge AJ, Daggett CW, Runge TM, Ungerleider RM, Calhoon JH. The type of aortic cannula and membrane oxygenator affect the pulsatile waveform morphology produced by a neonate-infant cardiopulmonary bypass

system in vivo. Artif Organs 1998; 22:681-6.
26. Ündar A, Calhoon JH. Stöckert roller pump generated pulsatile flow: cerebral metabolic changes in adult cardiopulmonary bypass [letter]. Perfusion 1998;13:215-6.
27. Ündar A, Fraser CD, Jr. The relation between pump flow rate and pulsatility on cerebral hemodynamics during pediatric cardiopulmonary bypass [letter]. J Thorac Cardiovasc Surg 1998;116:530-1.
28. Ündar A, Frazier OH, Fraser CD, Jr. Defining pulsatile perfusion: quantification in terms of energy equivalent pressure. Artif Organs 1999;23:712-6.
29. Shepard RB, Simpson DC, Sharp JF. Energy equivalent pressure. Arch Surg 1966;93:730-40.
30. Wright G. Mechanical simulation of cardiac function by means of pulsatile blood pumps. J Cardiothorac Vasc Anesth 1997;11:299-309.
31. Ündar A, Masai T, Frazier OH, Fraser CD, Jr. Pulsatile and nonpulsatile flows can be quantified in terms of energy equivalent pressure during cardiopulmonary bypass for direct comparisons. ASAIO J 1999;45:610-4.
32. Ündar A, Eichstaedt HC, Masai T, et al. Comparison of six pediatric cardiopulmonary bypass pumps during pulsatile and nonpulsatile perfusion. J Thorac Cardiovasc Surg 2001;122:827-9.
33. Lee JJ, Tyml K, Menkis AH, Novick RJ, McKenzie FN. Evaluation of pulsatile and nonpulsatile flow in capillaries of goat skeletal muscle using intravital microscopy. Microvasc Research 1994;48:316-27.
34. Ündar A, Eichstaedt HC, Bigley JE, et al. Effects of pulsatile and nonpulsatile perfusion on cerebral hemodynamics investigated with a new pediatric pump. J Thorac Cardiovasc Surg 2002;124:413-6.
35. Ündar A, Henderson N, Thurston GB, et al. The effects of pulsatile vs. non-pulsatile perfusion on blood viscoelasticity before and after deep hypothermic circulatory arrest in a neonatal piglet model. Artif Organs 1999;23:717-21.
36. Bellinger DC, Wypij D, duPlessis AJ, et al. Neorodevelopmental status at eight years in children with dextro-transposition of the great arteries: The Boston Circulatory Arrest Trial. J Thorac Cardiovasc Surg 2003;126:1385-96.
37. Mack MJ, Brown PP, Kugelmass AD, et al. Current status and outcomes of coronary revascularization 1999 to 2002: 148,396 surgical and percutaneous procedures. Ann Thorac Surg 2004;77:761-8.
38. Schoenburg M, Kraus B, Muehling A, et al. The dynamic air bubble trap reduces cerebral microembolism during cardiopulmonary bypass. J Thorac Cardiovasc Surg 2003;126:1455-60.
39. Groom RC, Likosky DS, O'Connor GT, et al. Identification of techniques associated with changes in embolic count, hemodynamics and cerebral desaturation. II. Perfusion [Abstract]. Heart Surg Forum 2003;6:205.
40. Holcomb HB, Stammers AH, Gao C, et al. Perfusion treatment algorithm: Methods of improving the quality of perfusion. J Extra Corpor Technol 2003;35:290-6.
41. Jegger D, Ruchat P, Horisberger J, et al. A cardiopulmonary bypass score system to assess quality of perfusion performance. Perfusion 2001;16:183-8.
42. Stammers AH, Mejak BL. An update on perfusion safety: does the type of perfusion practice affect the rate of incidents related to cardiopulmonary bypass? Perfusion 2001;16:189-98.