Getting it Right: Optimizing the Patient and Technique for the Procedure

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Abstract: The methodological approach to decision making in optimizing medical care has focused on using the best available evidence with the primary endpoint being patient outcome. Through this emphasis, quality becomes relegated as the quintessential factor in determining application of medical intervention and in directing resource allocation. When evidence is inconclusive or absent, then clinical judgment becomes elevated in the decision analysis schema. The paucity of well designed controlled trials in perfusion technology has resulted in a greater reliance on clinical judgment than published information. This has created an environment where significant variability exists throughout the perfusion community. The following report will discuss several reasons for this variability, and describe techniques where the preponderance of evidence is available supporting inclusion in perfusion practice. Keywords: optimized perfusion, extracorporeal circulation.

Optimization: An act, process, or methodology of making something as fully perfect, functional, or effective as possible; specifically: the mathematical procedures involved in this. (www.merriam-webster.com/dictionary/optimization).

The factors leading to a successful conduct of cardiopulmonary bypass (CPB) can be evaluated using various measures, but the paucity of focused well designed studies using sound scientific methodology hinders interpretation, making an evidence-based approach for decision analysis challenging. Regardless, the most salient outcome of a well applied CPB process is the improvement seen postoperatively in a patient’s quality-of-life. Although a great deal of research has been performed on assessing post-CPB outcomes, the vast majority of interest has focused on neuropsychological function. A significant body of evidence on extracorporeal circulation (ECC) has been derived from the numerous procedures and studies that have been performed on patients with atherosclerotic coronary artery disease. Improvements to both the CPB circuit and techniques of perfusion have come mainly from the study patients who have undergone CPB for coronary artery bypass grafting (CABG). These changes are then broadly applied to other cardiac disease states, both acquired and congenital, with few studies existing to confirm the efficacy of treatment in these patients who present with different co-morbidities and clinical challenges. The prevalence of coronary artery disease, and the number of CABG procedures, have both declined due to risk-factor reduction and to interventional techniques in the cardiac catheterization laboratory (1,2). However, predictions for future surgeries estimate an increase in the number of valvular and combined procedures requiring a reexamination of the applicability of techniques in this patient population. Recent efforts to identify optimized perfusion using an evidence-based approach, although well intended, will suffer from the lack of heterogeneity in the population of studied patients who may no longer reflect the acuity and disease states of future patients requiring CPB (3,4). Nevertheless, they do provide a basis by which future studies can be derived and serve an important reminder of the need for increased knowledge in perfusion.

During CPB perfusion is affected by a number of factors that can be broadly classified into the following categories: mechanical, technical, biological, or hemodynamic. Identifying methods for optimizing the conduct of perfusion is fraught with difficulty and is related to a number of factors including the diverse and varied response to ECC, the variation in perfusion technique, a lack of standardized protocols for mechanical perfusion of a tissue or organ, and inconsistencies in the monitoring and assessment of the adequacy of perfusion. Furthermore, the biological nature of the patient represents an independent factor that is often unpredictable and increases variation.

These factors, combined with the multifactorial nature of CPB, complicate efforts to identify key developments and advances in technology of perfusion. The following paper will focus on several areas of CPB that has either
shown to improve outcomes in patients undergoing CPB or to provide an opportunity for improved outcomes. The categories that will be addressed are mechanical circulation, perfusate composition, autologous priming, and miniaturization or “Stealth” perfusion circuitry.

MECHANICAL CIRCULATION

There are a number of mechanisms available to clinicians for the conduct of ECC. Pumping mechanisms for the movement of blood flow are classified into three major categories: Positive Displacement, Kinetic (centrifugal), and Axial and Pneumatic/Electric. Axial and pneumatic/electric pumps have been relegated almost totally to use as either short-term single-ventricle unloading devices or as ventricular assist devices for long-term perfusion and will not be discussed here. Positive displacement (roller pumps) and kinetic pumps (centrifugal pumps) remain the mainstay for routine clinical perfusion and are used almost equally in the United States (5).

Positive Displacement Pump

Clinicians have long touted the benefit of carefully controlled positive displacement pumping via the standard twin roller pump. Roller pumps move solution from suction discharge by the compression of a collapsible tube in a rigid raceway. Flow is dependent upon the length of the occluded tubing segment, the internal bore of the tubing, the degree of occlusion, and the number of revolutions per minute. Roller pumps have been made safer in recent years by the advancements to modern day heart-lung machines that incorporate safety mechanisms that include pressure regulation, bubble and level detection, and automatic line clamping with the use of a centrifugal pump. However, these systems are dependent upon the appropriate utilization of safety devices, which have been shown to be only intermittently used (6). One uncontroverted benefit of the roller pump over kinetic counterparts is the delivery of a pulsatile waveform. Although some systems for kinetic pumping offer this modality, centrifugal pump users rarely use them. The inherent non-occlusive aspect of the kinetic pump increases the risk of retrograde flow during the down cycle of the pulsatile waveform.

Kinetic Pumps

Kinetic pumps, also termed centrifugal pumps, offer a distinct and measurable advantage over roller pumps: They are preload dependent and will deprime when challenged with a large volume of air which may occur with the inadvertent emptying of the venous reservoir. During the past decade perfusionists have moved away from collapsible venous reservoirs for open (hard-shell) systems mainly for economic reasons (6). Centrifugal pumps when used with open-reservoirs, except in the case of augmented venous drainage (AVD), are in series with the atmosphere and therefore have the potential for air entrainment. Centrifugal pumps have been used in a variety of special perfusion situations. Their utility in left heart assist, isolated perfusion of independent vascular beds (cerebral, liver, renal, and splanchnic), and as rapid infuser device cannot be debated. However, their incorporation as a routine perfusion device is questioned due to the increased cost associated with their use. In our institution the use of a centrifugal pump adds approximately $95 to each procedure.

Kinetic Pumps vs. Roller Pumps

Kinetic pumps are especially beneficial during minimally invasive surgical procedures where peripheral cannulation sites are used usually with smaller venous cannulae (7). The use of AVD is facilitated either directly with the centrifugal pump (kinetic assisted venous drainage) or indirectly with vacuum (vacuum assisted venous drainage) (8). Investigators have shown that when a kinetic pump is used in combination with AVD there is an increased potential for the delivery of micro air emboli (9).

Neurological outcomes related to the type of perfusion system have been studied, but the results are equivocal. This is more than likely related to numerous factors including the variation in assessment techniques and the complexity of neurological monitoring. However, it seems that there may be a reduced tendency towards adverse neurological deficit seen with kinetic vs. roller pumps (10). This is probably not related to an upregulated inflammatory response due to the pump type, since Ashraf has shown an increase in pro-inflammatory markers with the use of a centrifugal pump in patients undergoing elective CABG surgery (11). Although some research exists promoting a hematological benefit of kinetic pumping in preserving cellular elements such as platelets (12), recent data has not been able to confirm this (13). Some researchers have linked decreased chest tube drainage following cardiac surgery with kinetic pumps.

Methods of modifying positive displacement pumps have incorporated collapsible circuitry in the arterial pump position. Such systems offer an increased level of protection similar to that afforded by kinetic pumps and deserve further exploration. No clinical studies exist that support their use in routine cardiac surgery (14).

Summary

- By themselves, the type of arterial pump heads has not been shown to be an independent predictor of improved outcome.
- Centrifugal pumps are inherently safer than roller pumps in reducing the risk of air embolism.
- The cost of centrifugal pumps has declined significantly over the last decade due to a fiercely competitive market.
PERFUSATE COMPOSITION

The composition and characteristics for perfusate formulation has been intensely studied during the 50 years since the first successful use of ECC for cardiac surgery. The standard in adult CPB has been to use clear or asanguineous solutions and supplement with allogeneic blood products only when anticipated resultant hemoglobin drops below a critical level, usually 7–8 g/dL. Asanguineous solutions are generally classified into two broad categories termed crystalloid and colloid (15). All CPB perfusates use a balanced physiologic buffered solution as the major prime component. However, the use of colloids as prime additives is still hotly contested which is complicated by the multitude of solutions available throughout the world (16–18). Colloidal solutions fall into two categories based upon their derivation. Synthetic colloids include starch and gelatin solutions while autogenous sources are from pooled albumin. Both have been used in priming solutions as volume expanders used to attenuate the extravasation of fluid and reduce the risk of interstitial fluid accumulation and edema (19). The transudation of plasma water and proteins increases the likelihood of edema and alters pharmacokinetic properties of administered drugs.

Albumin has been used both to coat the artificial surfaces of the extracorporeal circuit and to maintain colloid osmotic pressure (COP). The use of albumin in the prime solution pre-coats the surface of the circuit, which reduces adsorption of fibrinogen and may reduce activation and adhesion of platelets. Albumin binds many plasma proteins and lipids.

Hypoalbuminemia (3.0 g/dL) has been shown to be an independent predictor of increased mortality following CPB (20). Albumin levels of <3.5 g/dL have been shown to be the most powerful indicator of postoperative organ dysfunction (21). Some investigators have shown that for each standard deviation decrease in albumin there is an inverse relationship with mortality risk (22). The lower level of normality of albumin is 3.5 g/L with risk edema occurring when concentrations drop below 2.0 g/L. A COP of 15 mmHg or less in critically ill patients has been associated with less than a 50% survival rate (23).

Patients with serum albumin levels less than 2.5 g/dL have been shown to have 4-fold increase in morbidity and six times the risk of death when compared with patients with higher levels (24). In cardiac patients the majority of work has focused on clinical trials involving low risk patients. In these studies the effects of using albumin during cardiac surgery have been equivocal. However, the use of albumin supplementation in the critically ill has been shown to reduce both morbidity and mortality (25).

Albumin vs. Hetastarch

The question that is most challenging to clinicians remains what constitutes an effective colloidal solution and how do synthetic and autogenous solutions compare? Historically this question was predicated on the fact that synthetic solutions were much less expensive than human derived products. However, over the past several years the production of albumin has increased dramatically primarily as a result of the generation of immunoglobulin preparations that have as a “byproduct” albumin. This has generated a supply and demand market for albumin and has reduced the cost significantly from over 100 United States dollars per 50 mL bottle of 25% albumin to just under $35 in our institution. The cost of a 500 mL bag of 6% hetastarch is approximately $25. Such a dramatic price reduction has generated renewed interest in albumin as an alternative to hetastarch, which just a few years ago, was the impetus that drove the opposite comparison. Indeed, at Geisinger Health Systems, we have changed from 100% hetastarch users for cardiac patients to near total users of albumin. Comparative studies have shown that hetastarch is similarly effective in maintaining COP and reducing extravasation of plasma water as albumin (26). However, the caveat for the use of synthetic starches is their capacity to reduce hemostatic function, which has been shown to lead to increased chest tube output and bleeding in the postcardiotomy period (27,28).

Summary

- Priming solutions from CPB circuits should match physiologic conditions.
- The use of hetastarch, and other synthetic starch-based colloidal solutions, has been shown to be effective volume expanders during CPB.
- The use of hetastarch has been shown to impair hemostatic function in both healthy volunteers and in cardiac surgical patients and should be avoided in at-risk patients for bleeding.

AUTOLOGOUS PRIMING

Although the CPB apparatus has suffered by its depiction as an active participant in enhancing the sequelae associated with cardiac surgery, its critical requirement to be completely fluid filled makes it a model for fluid displacement. When the patient’s own volume is being used to displace the prime solution, the process is called autologous priming (AP). This technique was first described in the literature by Rosengart et al. from the New York Hospital-Cornell Medical Center but it had been practiced for years by perfusionists who removed volume prior to going on CPB and replaced it with the patient’s own blood (29). Rosengart et al. had shown that this technique reduces hemodilution and lowers the number of patients requiring red cell transfusions. Several groups have since reported similar results with higher hematocrits (30–34). One study concluded that AP did not offer a clinical benefit as a blood
conservation technique. However, the trial was a retrospective study that reported lower AP volumes than other successful studies (35).

One of the most beneficial aspects of AP is the fact that it requires no special equipment and can be performed on most patients. At our institution we contemplate performing AP on all individuals greater than 15 kg. Although AP can be achieved without difficulty the majority of time there are instances where its success is compromised. Patients with hemodynamic instability, those requiring higher filling volumes, and those whose starting hematocrit require the CPB circuit to be primed with allogeneic blood products should probably not undergo AP. Recently, we reported our results on 100 adult patients who underwent AP (36). We confirmed that the successful application of AP resulted in significantly higher hematocrits and lower transfusion rates, and the success was related to the degree of skill of the perfusionist and the communication amongst the operative team.

Summary
• Our use of AP resulted in significantly fewer allogeneic transfusions and higher on-CPB hematocrits.
• Given that the majority of reports, including all of the randomized trials, support the use of AP, the technique should be considered a standard blood conservation strategy during CPB.

MINIATURIZATION OF PERFUSION CIRCUITRY

One of the emerging trends in CPB has been an effort to reduce the impact that the extracorporeal circuit has on the morbidity associated with CPB and cardiac surgery. The modification of CPB circuit surfaces by coatings and treatments to reduce the systemic inflammatory response is gaining popularity but has not been universally accepted. Efforts to reduce circuit prime volumes and further reduce hemodilution are generally embraced as has been described with AP. The reduction in hemodilution should lower both anemia and allogeneic transfusion risk. Efforts to reduce the imprint of CPB have focused at reducing total surface area, and hence concomitant prime volume. One mechanism to achieve this reduction would be to use the patients vascular system as the venous reservoir and use assisted venous return as a means to achieve drainage, and hence, adequate flow. This type of CPB has been termed “mini-bypass” or more appropriately “stealth perfusion.”

One of the earliest commercial attempts to miniaturize bypass circuitry was the development of an integrated pump-oxygenator as a single perfusion system without accessory pumps for aspiration and venting (CORx System™, CardioVention, Inc., Santa Clara, CA). The system used an integrated pump-oxygenator that used a centrifugal pump to kinetically drain venous blood from the patient. There was an air evacuation system for the removal of air from the venous line that was entrained around purse string sutures or during the inadvertent opening of the right atrium or cavae to atmosphere. Temperature was controlled by an optional heat exchanger that could be placed in the arterial line leading to the patient. All shed blood, vented blood, and blood removed during air evacuation was discarded or sent to a cell washing system. The primary benefit of the system was a reduced surface area with an oxygenator bundle of 1.1 m². An ultrasonic device detected air in the venous line proximal to the centrifugal pump, which activated the air evacuation system that aspirated air to a collection reservoir. Several authors evaluated this device and found a significant reduction in prime volume when compared with conventional CPB systems and lower release of inflammatory mediators (37–39). However, there were a number of problems that quickly became apparent when closed perfusion systems were used. These included reduced margins of safety in handling volume loss, increased blood loss, and increased potential for air embolism (40). Perhaps most challenging, significant modification in the conduct of CPB was required when using a kinetically assisted closed system. For these reasons the CORx™ System did not gain support and is no longer manufactured.

However, the principles of stealth perfusion are gaining momentum, and several cardiopulmonary companies have developed miniaturized CPB systems: Minimal Extracorporeal Circulation System (MECC), Jostra AG, Hirrlingen, Germany; Performer™ Medtronic Cardiopulmonary, Minneapolis, MN; Synergy, Sorin Biomedical, Arvada, CO) (41,42). Both the Medtronic and Jostra systems use traditional extracorporeal components that have been modified to perform closed system CPB. However, the Sorin Synergy™ uses a unique oxygenator design that incorporates a centrifugal pump, oxygenator, and arterial line filter.

Stealth perfusion techniques will likely continue to develop and expand. Perhaps the center with the greatest experience with this technology is the Istituto Policlinico in Milan, Italy where Ranucci has published extensively on their experience (43–45). These researchers have shown that the successful use of mini-bypass circuits has resulted in a significant improvement over standard CPB techniques with patients demonstrating reduced morbidity. The changes in cardiac surgery patients (i.e., increasing preoperative risk, increasingly complex operative requirements) and changes in the demand for CPB have collided with an increased knowledge base and an expanded appreciation for the physiology of CPB. These elements compliment the need for improving the conduct of CPB. Stealth perfusion—including reducing allogeneic transfusions and anemia through improved perfusion techniques and technology, concurrent with surface modification and
decreased surface area to reduce the systemic inflammatory response—should continue to be embraced.

CONCLUSION

The conduct of ECC must continuously be improved to reduce the sequelae associated with its application. Knowledge of mechanisms that have been shown to improve outcomes must be translated into action and incorporated in clinical care plans modified for the individuality inherent in each patient. This can only be done through the combined effort of making the synthetic devices and equipment more benign to the human immune system, and by improving the physiological basis of how bypass is conducted. As with most technological advances, those that benefit the most will be those who are most in need.

“There is something fascinating about science. One gets such wholesale returns of conjecture out of such a trifling investment of fact.”

Mark Twain, 1835–1910

REFERENCES


