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Advantages to Miniaturized Cardiopulmonary Bypass for Adult Cardiac Surgery

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The development of cardiopulmonary bypass (CPB) and open heart surgery in the 1950s has benefited millions of people around the world over the last half century. However, it has been recognized since the beginning that there are detrimental effects to CPB. In an effort to minimize the effects of CPB, a miniaturized CPB (M-CPB) closed circuit system also known as closed circuit extracorporeal circulation (CCECC) has been developed as a strategy. In this review, we will look at the rationale behind the development of the miniaturized cardiopulmonary bypass circuits, the published results in comparison to both conventional CPB (C-CPB), and off pump Coronary Artery Bypass Grafting (OPCAB), and the surgical and perfusion strategies to incorporate this technique into everyday adult cardiac surgical practice.

The deleterious effects of CPB have been well described including complement and white blood cell activation with a systemic inflammatory response resulting in renal, hematologic, pulmonary, and neurologic effects [1]. The inflammatory response is partially explained by blood contact with the artificial surface of the bypass circuit [2]. There are disturbances in the coagulation cascade which contribute to the need for transfusion of blood products. Post operative atrial fibrillation, one of the most common complications after cardiac surgery, is thought to be related to CPB [3]. M-CPB reduces the artificial surface for blood contact with less of a resulting inflammatory reaction [4].

The cardiac surgery market has seen a number of new products over the last decade designed to improve the quality of CPB. This includes non-heparin based biocompatible treatments, new generation centrifugal pumps, and minimized circuit CPB equipment. There are a number of different M-CPB systems available commercially. This includes the following: the Resting Heart System (RHS; Medtronic Inc., Minneapolis, MN); the Minimized ExtraCorporeal Circulation (MECC) System (Maquet Getinge Group; Hirrlingen, Germany); the Ecco and Synergy system (Sorin Group; Milan, Italy); the ROCSafe™ Hybrid Perfusion System (Terumo; Ann Arbor, MI); and the CORx system (CardioVention; Santa Clara, CA).

Common Features to M-CPB

Harling [5] outlines a number of common features that these M-CPB circuits utilize which will be discussed. First, a heparin/phosphorylcholine/polymer coated tubing to reduce protein adsorption and platelet activation. Second, low prime volumes (500-800 cc compared to 1500cc in C-CPB) so that a combination of reduced tubing area and reduced priming volume can minimize hemodilution. Hemodilution during CPB leads to reduced levels of coagulation and fibrinolytic proteins. Using a lower priming volume has been shown to reduce transfusions by about 30% [6]. Finally, hemodilution has been implicated as a major factor in organ dysfunction, short-term mortality, and long-term morbidity [7].

Third, the lack of a venous cardiotomy reservoir removes the foreign blood-air interface and avoids stasis in the reservoir thus reducing clotting factor and inflammatory mediator activation. Reinfusion of cardiotomy suction blood exposed to pericardial surfaces is associated with postoperative neurologic injury secondary to increased levels of hemolysis and fat in scavenged blood [8]. Fourth, a centrifugal pump actively draining the right atrium to reduce platelet aggregation and cellular damage. Fifth, cell salvage so that all blood shed from the operative field is removed by a cell saver system. This blood can then be washed and re-transfused. Sixth, kinetic assist to augment venous drainage coupled with venous line air handling devices and arterial line filters to reduce venous air entrapment add safety to the circuit by reducing the chance of air embolization.

The literature comparing M-CPB to C-CPB is limited by the small sample sizes in most studies. Indeed, there are only three with more than 100 patients randomized in each arm [9-11]. (Table 1) is a comparison of these three larger randomized trials with at least 100 patients comparing M-CPB to C-CPB. Two of the studies [9,10] demonstrate a clear benefit with respect to bleeding and transfusion either in the OR, the first 24 hours, or in actual reoperations for bleeding. After isolated CABG with conventional CPB (C-CPB) it has been well demonstrated in large studies that perioperative red blood cell (RBC) transfusion is an important factor in postoperative mortality, infection, ischemic postoperative morbidity, hospital stay, and hospital costs [12]. Of further concern, is that in an analysis of over 10 thousand patients who underwent CABG, it was demonstrated that each unit of RBC transfusion is associated with an incremental reduction in risk-adjusted survival in both the early phase (up to six months after surgery) and the late phase (out to ten years) [13].

There have been two meta-analyses of randomized trials of M-CPB to C-CPB with similar conclusions. Benedetto [14] looked at 11 papers and Biancari [15] looked at 13 papers (7 were common to both).

Benedetto's [14] analysis focused specifically at 1051 patients for RBC utilization in CABG patients. This metaanalyses found that M-CPB was associated with reduced RBC transfusion and a reduction in the amount of RBCs transfused. Although some studies failed to show a benefit, the majority of these studies had very small numbers with 3 out of 7 having fewer than 10 patients in each arm.

Biancari's [15] analysis of 1161 patients looked at additional outcomes. Notably, they found that there was a trend for a reduction in mortality in the M-CPB group (1.1%) compared to the C-CPB group

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						Low CO	Intra Op	PRBC in	Reop for	LOS	Afib	MI
		Patients	Procedures	Mortality	Stroke	Syndrome	Transfusion	first 24 hrs	Bleeding			
El-Essawi	M CPB	252	CABG 75%	1 (0.4%)	2 (0.8%)				* 2.4%	*10.3 4.8%	*14 (16.3%)	*4 (1.6%)
Perfusion 2011			AVR±CABG 25%									
Germany	C CPB	248	CABG 76%	3 (1.2%)	2 (0.8%)				* 6.1%	*11.8 6.8%	*60 (24.2%)	*13 (5.2%)
			AVR±CABG 24%									
Remadi	M CPB	200	CABG	1.50%		* 0.66%	* 6%					
Am Heart J 2006												
France	C CPB	200	CABG	2.50%		* 4%	* 12.8%					
Abdel-Rahman	M CPB	101	CABG					245 ± 398				
Ann Thor Surg 2005												
Multinational	C CPB	103	CABG					184 ± 384				

*p<0.05
CO= Cardiac Output
PRBC= Packed Red Blood Cell
MI= Myocardial Infarction
LOS = Length of Stay

Table 1: Comparison of three larger randomized trials with at least 100 patients comparing M-CPB to C-CPB.

(2.2%, p=NS). It is important to put into context that contemporary results for CABG are excellent with a mortality of 1.8% in over 1.5 million patients analyzed in the Society of Thoracic Surgeons (STS) database [16]. Thus, studies would have to enroll thousands of patients to be able to determine a clinically significant reduction in mortality in low-risk CABG patients. It is perhaps more important to demonstrate that M-CPB does not add increased mortality risk to CABG than to actually claim a mortality benefit.

The same rationale would apply to stroke. Namely, to demonstrate that air embolization or other events did not result in an increase in stroke in the M-CPB group. However, what is even more profound from Biancari's analysis was that there was actually a significant decrease in the incidence of stroke in the M-CPB group (0.2%) compared to the C-CPB (2%) group. In one study to attempt to explain this finding, measurement of cerebral oxygenation by near-infrared spectroscopy was used to compare M-CPB and C-CPB [17]. A significantly lower oxyhemoglobin in the C-CPB was noted compared to the M-CPB. In addition, M-CPB had a significantly lower total embolic count (733 ± 162) compared to the C-CPB (1591 ± 555, p<0.02) group.

Given that stroke is often cited as the most feared complication of CABG surgery, the low stroke incidence compares very favorably with the generally accepted 1-2% incidence after CABG [18,19]. Indeed, in the landmark SYNergy between PCI with TAXus and Cardiac Surgery (SYNTAX) trial (Boston Scientific; Natick, MA) the 30-day stroke rate in the CABG arm was 1.0% and 2.2% at one year [20]. Thus, while the SYNTAX trial endpoints favored surgery, many physicians focused on the higher CABG stroke rate. Thus, all surgical techniques that may reduce the incidence of stroke should be considered to preserve the role of CABG in coronary revascularization.

Finally, in the four studies that analyzed the incidence of postoperative atrial fibrillation, Biancari's analysis [15] found that the M-CPB group (29.6%) had a lower incidence compared to C-CPB (34.9%) group. Atrial fibrillation (AF) has been shown to occur in over 30% of patients after CABG [21]. AF is associated with greater in-hospital mortality, stroke, hospital length of stay, and myocardial infarction. At five years, long term survival was worse (74 vs. 87%, p<0.0001) [22] in patients who developed AF after CABG.

The development of OPCAB in the 1990s was a direct response to providing an alternative to CPB. Although a number of different explanations have been offered including concerns over incomplete revascularization and long-term graft patency, inconclusive evidence of reduced neurologic injury, and technical challenges associated with a steep learning curve, OPCAB in the United States represents no more than 20-25% of all CABGs performed. Thus, CABG with CPB and cardioplegic arrest remains the standard of care for most cardiac surgeons.

Although there are no large multicenter randomized trials comparing OPCAB to M-CPB, there are smaller studies that demonstrate comparable benefits. Formica [23] demonstrated in a 60 patient randomized study dividing patients to OPCAB and M-CPB similar results between the two groups in terms of systemic inflammatory response mediators (IL-6, TNF-α), myocardial inflammation, and early outcomes. In a comparison of M-CPB with C-CPB and OPCAB, in a small study of 10 patients in each arm, the reduction in red blood damage and activation of coagulation cascades are similar between OPCAB and M-CPB [24].

Thus, which patients might especially benefit from M-CPB? In a propensity score matched group, Rimpilainen et al found that the efficacy of M-CPB was more pronounced the more complex the cardiac surgical procedure that necessitated longer perfusion times [7]. This is similar to large analyses that demonstrate that the benefit in OPCAB is in high risk patients [25]. In certain higher risk clinical situations, beating heart support with M-CPB has been described [26]. M-CPB has also been described for minimally invasive valvular heart surgery [27]. We have used it in multiple valve and circulatory arrest cases. In Great Britain, M-CPB has become increasingly popular and is used in up to 40% of centers [28].

M-CPB Techniques

Well-conducted cardiac surgery involves excellent communication amongst the surgeon, perfusionist, and anesthesiologist. It is even more vitally important with use of M-CPB. In our experience with the Resting Heart System (Figure 1) similar to other M-CPB systems, close attention to the blood pressure is required during the retrograde autologous priming (RAP). Before onset of CPB, all patients receive 400 IU/kg of heparin intravenously to maintain an activated clotting time more than 480 seconds during CPB which is identical to our C-CPB practice. Because the circuit has been primed with a lower volume of the patient's blood (typically around 2 L but with RAP it is closer to 1 L), careful attention is required during initiation of CPB. Combining

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Figure 1: Resting Heart System.

M-CPB with RAP allows for a higher intraoperative hematocrit. We aim to keep the central venous pressure (CVP) close to normal which does not result in washout of cardioplegia. Our goal is to maintain a cardiac index of 2.4L/min/m^2 although it is not uncommon to fall just short of that mark. We do, however, utilize near-infrared spectroscopy or NIRS (Fore-Sight Cerebral Oximeter, Cas Medical Systems, Branford, CT) to monitor brain desaturation episodes routinely and use that information to help determine the adequacy of pump flow [29].

Kinetic assist is required so emptying the heart with decreased perfusion flow may be a challenge. It is necessary to ensure a complete seal around a properly positioned venous cannula to prevent air entry. We are liberal in our use of additional pursestring sutures around the venous cannula if needed. The surgeon needs to observe the heart closely to ensure that the right atrium and ventricle are emptied and manipulation of the venous cannula to optimize drainage is occasionally necessary. Finally, cardiac manipulation such as pulling the heart for distal coronary artery anastomoses to the lateral wall or left atrial traction during mitral valve surgery may impede venous drainage and lower perfusion flows [30]. Since there is no venous reservoir, the patient's venous vasculature is effectively the "reservoir" by utilizing vasoactive drugs to promote vasodilation and increase capacitance.

A surgeon wishing to begin using M-CPB is advised to begin with low risk CABG patients with adequate BSA (body surface area). In our experience, the most challenging patients are small females undergoing aortic valve replacement for aortic stenosis with severe concentric left ventricular hypertrophy. In the ICU, that patient is likely to be volume depleted with labile BP requiring gentle volume hydration.

Conclusion

Miniaturized CPB offers genuine advantages with respect to blood product utilization and encouraging results from a safety profile. In a large evidence-based review of the practice of CPB in adults [31], the authors recognized the effective attenuation of the systemic inflammatory response by reduction of the circuit surface area and use of biocompatible surface-modified circuits with miniaturized CPB and gave a Class IIA (Evidence Level B) recommendation. As patients become more informed about avoiding blood transfusions, the imperative to provide improved perfusion strategies will continue to grow. Since off pump CABG is not the preferred technique for most surgeons for CABG, it is reasonable for surgeons to consider "better bypass" with utilization of miniaturized cardiopulmonary bypass circuits.

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