The Heart Surgery Forum #2002-15534
5 (3):221–224, 2002

Online address: www.hsforum.com/vol5/issue3/2002-15534.html

Hemodynamic Changes During Cardiac Manipulation in Off-CPB Surgery: Relevance in Brain Perfusion

(#2002-15534 … March 15, 2002)

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ABSTRACT

The recent introduction of various cardiac stabilization and positioning devices, alone or in combination with deep pericardial traction sutures, has greatly increased the ability to perform beating heart surgery to accomplish multi-vessel coronary revascularization without the need for cardiopulmonary bypass (CPB), with its associated risks. However, positioning the heart for anastomosis of the circumflex (Cx) and the posterior descending artery poses a risk of inducing hypotension, impaired cardiac output, and generalized hemodynamic instability with risk of cerebral compromise. This report discusses clinical studies suggesting that compromised right ventricular diastolic filling as a result of direct ventricular compression, rather than impaired contractility or ischemia, may be the primary mechanism for producing hemodynamic instability during OPCAB surgery. Foremost among measures to minimize ventricular compression is optimal placement of the myocardial stabilization device. Secondary measures include steep Trendelenburg positioning, fluid loading, right-sided pleuro-pericardial window that allows rotation of the heart by partial herniation into the right pleural cavity, and possibly certain pharmacological agents. This report also analyzes the effect that variable degrees of hemodynamic disturbance accompanying displacement of the heart for OPCAB surgery has on end-organ perfusion and considers the effects of hypotensive agents, direct cerebral dilators, and patient-specific factors on cerebral blood flow. The role of the partial aortic occlusion clamp and risk of stroke is also considered. We conclude that for cardiac surgery patients considered at increased risk of adverse central nervous system events, direct monitoring of cerebral function and avoidance of aortic manipulation is strongly recommended.

Presented at the Fifth International Symposium on Total Myocardial Revascularization Without Cardiopulmonary Bypass, Tampa, FL, March 15-16, 2002.

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INTRODUCTION

The recent introduction of various cardiac stabilization and positioning devices, alone or in combination with deep pericardial traction sutures, has greatly increased the ability to perform multi-vessel coronary revascularization during beating heart surgery with avoidance of cardiopulmonary bypass (CPB). Preliminary evidence, largely from a group of patients undergoing single-vessel minithoracotomy, had suggested that avoidance of CPB was associated with improved outcomes relative to conventional coronary artery bypass grafting (CABG) [Murkin 1999b]. Most recently, however, Van Dijk et al. have reported results with 281 patients undergoing multi-vessel coronary revascularization who were randomly assigned to off-pump coronary artery bypass (OPCAB) or CABG [Van Dijk 2002]. They reported no statistically significant difference in the incidence of cognitive decline between the OPCAB and the CABG groups (21% vs. 29% respectively, $p = 0.15$), although a significantly greater improvement in cognitive performance (i.e., learning effect) was seen in the OPCAB patients ($p = 0.03$) at three months. It is clear that, during OPCAB, positioning the heart for anastomoses of the circumflex (Cx) and posterior descending arteries poses a risk of inducing hemodynamic instability with potential compromise of cerebral perfusion, and that "blind" usage of a partial occlusion clamp on the aorta may largely negate any stroke-related benefit of avoiding CPB.

DISCUSSION

Hemodynamic Changes

In performing multi-vessel coronary revascularization on the beating heart, patient-specific factors such as myocardial dilatation, low ejection fraction, and presence of mitral regurgitation mandate extra caution and the ready availability of inotropic agents and standby CPB support. In such patients, selective right heart bypass may be especially useful (see below). Secondary measures that are variously advocated, such as steep Trendelenburg positioning and fluid loading, function to increase venous return and augment right ventricular filling pressures, thereby maintaining hemodynamic stability. Right-sided pleuro-pericardial window allows rotation of the heart by partial displacement into the right pleural cavity, thus improving ventricular compliance and facilitating right ventricular ejection. Implicit in all these measures is the absolute necessity for optimal placement of the myocardial stabilization device to minimize ventricular compression. A

few extra moments spent in ensuring the best epicardial exposure with the least amount of ventricular compression will usually eliminate or greatly reduce the need for additional retraction or use of ventricular slings and ties—measures frequently associated with progressive hypotension, decreased cardiac output, and generalized hemodynamic instability.

By using transesophageal echocardiography (TEE), in conjunction with continuous cardiac output pulmonary artery and radial artery catheters, Biswas et al. made a clinical assessment of myocardial performance during myocardial displacement using the Octopus® stabilizer for Cx grafting [Biswas 2001]. They demonstrated that reversible left ventricular wall motion abnormalities were present significantly more during Cx territory grafting, associated with both regional systolic dysfunction and restrictive diastolic filling, which indicates decreased left ventricular compliance. Using direct left atrial and left ventricular catheters and an Octopus® stabilizer, Mathison et al. demonstrated that the greatest increases in both left and right ventricular end-diastolic pressures (RVEDP) occur during positioning for Cx grafting [Mathison 2000b]. Simultaneously, mean arterial pressure (MAP) decreased 22%, stroke volume decreased 28%, and cardiac output fell 37%, while left and right atrial pressures (LAP, RAP) increased by 59% and 168%, respectively. They also demonstrated that increases in RVEDP occur even with minimal myocardial displacement for left anterior descending artery exposure. They further demonstrated that Cx displacement caused moderate to severe compression of both ventricles. Left ventricular cavity size was diminished considerably, the left atrium was enlarged, and both the right atrium and ventricle were compressed.

Both of these clinical studies have demonstrated that compromised right ventricular diastolic filling as a result of direct compression, reflected as decreased compliance with increased pressure at decreased volume, appears to be the primary mechanism producing hemodynamic instability during OPCAB surgery. Using ultrasound transit time flow probes, other studies have demonstrated that there is minimal or no direct mechanical obstruction of coronary flow due to verticalization of the heart, attributing the observed decreases in cardiac output (CO) to direct ventricular compression rather than impaired contractility or ischemia [Burfeind 1998, Grundeman 1998]. Consistent with these observations, right heart-assist devices have been demonstrated to improve hemodynamics during myocardial displacement for Cx grafting [Grundeman 1999, Mathison 2000a], whereas left heart bypass failed to restore systemic circulation [Grundeman 1999]. It should be noted, however, that excess flow through right-heart bypass can paradoxically decrease MAP and potentially may produce pulmonary edema, especially in patients with left ventricular failure, if too much flow results from the right side [Mathison 2000a].

These studies also support and explain the efficacy of many empirical clinical measures. Techniques aimed at augmenting ventricular filling, for example steep Trendelenburg positioning and fluid loading, would appear to be appropriate provided that RAP and RVEDP do not increase excessively (<20 mmHg) resulting in a secondary decrease in coronary perfusion pressure. Right-sided pericardectomy and minimizing the degree of ventricular compression act to improve ventricular compliance and enhance diastolic filling. Whether pharmacological measures aimed at specifically improving right ventricular performance through improved compliance and enhanced emptying would be beneficial has not been systematically investigated. Clinical studies have demonstrated that, unlike procedures performed using CPB in which downregulation or desensitization of ß-receptor function has been demonstrated [Booth 1998], there is no such ß-adrenergic dysfunction detectable during OPCAB procedures [Eldrup 2001]. It is thus likely that selective use of agents such as intravenous nitroglycerin, which improves ventricular compliance while it decreases pulmonary vascular resistance, or amrinone, which will in addition directly augment ventricular contractility, may be especially beneficial in OPCAB given that right ventricular dysfunction appears to be the primary etiology of the observed hemodynamic instability. Further, by using TEE to assess coronary blood flow velocity, it has been shown that during profound hypotensive anesthesia using nitroglycerin to decrease systolic arterial pressure to 60-70 mmHg, coronary blood flow velocity increased significantly by over 40% [Mikhail 2000].

Organ Perfusion

Given that variable degrees of hypotension and decreases in cardiac output accompany displacement of the heart for OPCAB surgery, what is know about the consequences of these hemodynamic disturbances on end-organ perfusion? Extrapolating from other types of surgery employing hypotensive anesthesia techniques is difficult since decreases in blood pressure as a consequence of vasodilator administration are generally associated with an increase in cardiac output as a consequence of lowered vascular resistance. This is confounded in OPCAB surgery, however, as decreased MAP is often due to decreased CO. As has been shown during CPB, however, there is evidence that with decreases in CO the brain will be preferentially perfused [Murkin 1987], provided cerebral autoregulation is preserved (see below).

Further, depending on whether the specific agents employed for hypotension have an independent direct effect on cerebral blood flow (CBF) (e.g., nicardipine, nitroglycerin, nitroprusside, and prostaglandin E1) or on both CBF and cerebral metabolic rate (CMR) (e.g., thiopental, propofol, and isoflurane), the results will vary. Additionally, patient-specific factors, including age, history of hypertension, intracranial and extracranial vascular disease, brain injury, brain temperature, and $PaCO_2$ and blood oxygen content, will all influence the cerebrovascular response to a given degree of hypotension.

As first demonstrated by Kety and Schmidt more than 50 years ago [Kety 1945], in normal awake individuals CBF autoregulates to maintain constant CBF at a perfusion pressure varying between 50 and 150 mmHg. This means that the resistance vessels of the brain will progressively vasodilate or vasoconstrict to allow sufficient but not excessive amounts of blood (substrate) to maintain tissue metabolism. This is termed flow/metabolism coupling and occurs at both a regional and a global level. It is the hallmark of a normally functioning brain. What has also become increasingly apparent is that the cerebral "autoregulatory plateau," that constant level of cerebral

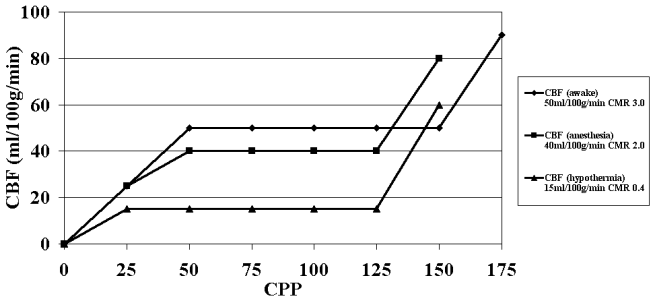

Figure 1. Cerebral Pressure/Flor Autoregulation

blood flow that is maintained over a range of perfusion pressures, is dependent on the CMR. As shown in Figure 1 (◎), awake individuals have a high autoregulatory CBF because their CMR is higher than for unconscious or anesthetized patients, in whom CMR and thus CBF is significantly lower, with hypothermic patients having the lowest autoregulatory plateau as a consequence of greatly reduced CMR [Murkin 1989]. This means that lower perfusion pressure can be tolerated during anesthesia, particularly if CMR is also decreased, as it is during isoflurane or propofol anesthesia.

Agents that are direct cerebral vasodilators, for example nicardipine, $PaCO_2$, and nitroprusside, will all potentially increase CBF by causing progressive cerebral vasodilation. While this may initially appear to be beneficial, it does indicate that cerebral autoregulation is impaired, thus disrupting the ability of the brain to selectively increase flow to ischemic areas. During hypotension, this may instead result in diversion of blood away from ischemic zones into preferentially perfused areas, a process known as "intracerebral steal," thus paradoxically increasing CBF while producing regional cerebral ischemia. This is an especial risk in patients with cerebral vascular disease. Unfortunately, such patients comprise a high percentage of those undergoing coronary revascularization [Baird 1997].

It has recently been demonstrated that during propofol-fentanyl anesthesia, cerebral pressure autoregulation in response to phenylephrine challenge was preserved during nitroglycerin-induced hypotension, in contrast to nicardipine [Endoh 2002], and nitroglycerin may thus be a beneficial choice for use during OPCAB. This is further corroborated by a study using gastric tonometry to assess splanchnic perfusion during hypotension induced by either isoflurane or esmolol and nitroglycerin, in which deliberate hypotension with either technique was not shown to compromise splanchnic tissue oxygen balance [Andel 2001]. In an interesting study of aged hypertensive rats, nitroglycerin moderated the decreases seen in CBF and CMR during hypotensive challenges, in contrast to nitroprusside-induced hypotension, leading the authors to speculate that nitroglycerin may decrease the risk of stroke more than nitroprusside during hypotensive anesthesia [Hoffman 1982]. These results must be interpreted cautiously, however. In a recent report of outcomes after controlled hypotension using isoflurane/propofol anesthesia for orthognathic surgery, there was evidence of increased adenylate kinase activity in cerebrospinal fluid that has been associated with abnormalities on postoperative psychometric testing, raising questions about cerebral perfusion and the safety of deliberately inducing hypotension [Frithz 1999].

Increased attention must also be paid to the hemodynamic changes and decreases in cerebral perfusion that are seen during OPCAB as greater degrees of myocardial displacement become necessary for more extensive myocardial revascularization. Maneuvers such as steep Trendelenburg positioning to access the posterior coronary circulation have been shown to increase jugular venous pressure, potentially compromising cerebral blood flow independent of whether an otherwise acceptable mean arterial pressure is maintained [Avraamides 1996]. Significant decreases in cardiac output, whether due to arrhythmias, dislocation of the heart, subclinical ischemia, or some combination of these, may significantly compromise blood flow to the brain [Malheiros 1999].

Partial Aortic Clamping

Today, most beating heart surgery operations are done as multi-vessel OPCAB procedures, which employ the use of a partial aortic clamp to perform proximal anastomoses. Yet the literature has repeatedly demonstrated that clamp application and removal is the greatest source of embolic activity during surgery and that the number of cerebral emboli is closely linked to subsequent adverse neurologic outcomes. In a series of studies by Barbut et al., over 58% of the emboli generated in cardiac surgery occur during clamp manipulation of the ascending aorta [Barbut 1997]. In a study of heparin-bonded circuits using transcranial Doppler to detect cerebral emboli, Aldea et al. demonstrated that release of the partial aortic clamp was associated with the greatest number of emboli [Aldea 1997]. While their data was obtained during CPB for CABG, a similar mechanism is likely operative during beating heart surgery, particularly since the partial aortic clamp is usually applied during maintenance of systemic mean arterial pressure. Until some method of either avoiding aortic instrumentation entirely, detecting and avoiding non-calcific aortic atheroma (such as epiaortic scanning (EAS)), or avoiding partial aortic clamping is incorporated into beating heart procedures, it appears less likely that there will be significant improvements in overt neurological complications associated with multi-vessel revascularization. Proof of this concept has recently been provided by Calafiore and colleagues who reviewed their experiences with 4,875 patients undergoing either CABG or OPCAB with and without the use of a partial aortic clamp [Calafiore 2002]. They demonstrated that in patients with extracoronary vasculopathy undergoing OPCAB procedures without the use of EAS, employment of aortic side-clamping was associated with the same CVA risk as observed in patients for whom CPB, aortic cannulation, and cross-clamping were used.

Use of EAS may alter this risk because it provides accurate images of the aortic wall and lumen and allows for optimization of cannulation or clamp sites. In a study of 102 patients in whom epiaortic scanning was performed directly after conventional aortic assessment by surgical palpation, in 23.5% of the patients aortic scanning resulted in a change in surgical management of aortic instrumentation by relocation of clamp or cannulation sites [Murkin 2000]. EAS was also associated with a significantly lower incidence of cerebral emboli result-

ing from cannulation and release of the aortic cross-clamp and partial clamp [Murkin 1999a].

CONCLUSION

For cardiac surgical patients considered at increased risk of adverse central nervous system (CNS) events, direct monitoring of cerebral function is recommended, particularly if episodic or prolonged hypotension is anticipated. Use of the stroke risk index scale can aid in the selection of patients deemed at greatest CNS risk [Newman 1996]. Multimodality CNS monitoring using combined measures of cortical activity (e.g., electroencephalography), cerebral blood flow (e.g., transcranial Doppler), and cerebral oxygenation (e.g., jugular venous oxygen saturation and non-invasive optical spectroscopy) is recommended [Luney 1997]. Some centers have undertaken such monitoring techniques and report good outcomes for OPCAB surgery [Novitzky 2000]. Techniques designed to avoid use of the partial aortic occlusion clamp, especially in the absence of EAS, should be encouraged. The results of studies specifically assessing CNS results using these techniques are awaited.

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