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Impact of Aortic Manipulation During Coronary Artery Bypass Surgery: The Effect of Aortic Clamping Strategies on Postoperative Stroke

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Abstract Cover Page

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By Michael E. Halkos

M.D. Emory University, 1999

B.A. University of Virginia, 1993

Advisor: John D. Puskas, MD

An abstract of

A thesis submitted to the Faculty of the James T. Laney School of Graduate Studies of Emory University in partial fulfillment of the requirements for the degree of Master of Science in Clinical Research, 2012

Abstract

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By
Michael E. Halkos, MD

Objectives: The purpose of this study was to determine the impact of different aortic clamping strategies during coronary artery bypass graft surgery (CABG) on incidence of postoperative stroke.

Methods: In this case-control study, all patients at Emory hospitals from 2002-2009 (N=140) with postoperative stroke after isolated CABG were matched 4:1 to a contemporaneous cohort of patients without postoperative stroke (N=565). Patients were matched according to the Society of Thoracic Surgeons (STS) Predicted Risk of Postoperative Stroke (PROPS) based on 26 variables. On- and off-pump CABG patients were matched separately. Operative notes were reviewed to document operative technique. Multiple logistic regression analysis with adjusted odds ratios (OR) was performed to identify operative variables associated with postoperative stroke.

Results: Within the on-pump CABG cohort, the single cross-clamp technique was associated with a decreased risk of postoperative stroke compared to the cross clamp and partial clamp (double clamp) technique (OR=0.385, p=0.044). Within the off-pump cohort, no significant difference was found between partial clamping and no clamping. In 2002, 47/86 patients (54.6%) did not have epiaortic exam performed, compared to only 7/66 (10.6%) in 2009. Epiaortic ultrasound grading was performed in 525 patients (74.4%): 75(14.3%) had grade 3-5 and 450(85.7%) had grade 1-2 aortic disease. In patients with epiaortic grades 3-5, a clampless technique was used in 59.5%, 83.3%, and 93.3% of cases, respectively. In patients with epiaortic grades 1-2, clampless techniques were used in 3.8% and 7.8%, respectively. No grade 5 patients had a postoperative stroke. Clamp use in general trended downwards from 97.7% of cases in 2002 to 72.7% of cases in 2009.

Conclusions: Aortic clamping during CABG may increase the risk of postoperative stroke. Epiaortic ultrasound use has trended upwards from 2002 to 2009, indicating a greater awareness of potential complications from aortic clamping and allowing for changes in operative technique. A single cross-clamp strategy was associated with a lower risk of postoperative stroke compared to the double clamp strategy in on-pump patients. Using a no clamp technique may reduce the risk of postoperative stroke in off-pump patients with grade 3-5 aortic disease by eliminating the need for aortic clamping during CABG.

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ABSTRACT

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INTRODUCTION

Coronary artery bypass surgery (CABG) continues to be one of the most

commonly performed operations in the world. Coronary artery disease (CAD) afflicts millions of Americans, and although significant advances have been made with medical treatment and percutaneous coronary intervention, surgical treatment is still the preferred approach for patients with multivessel and/or complex disease. Although outcomes are generally excellent after CABG, one of the most dreaded complications is postoperative stroke.

In March 2009, the latest randomized prospective trial comparing coronary artery bypass surgery to percutaneous coronary intervention was published(1). In this trial which investigated outcomes in patients with severe coronary artery disease, percutaneous coronary intervention was associated with higher rates of major adverse cardiac or cerebrovascular events at 12 months, largely because of the increased rate of repeat revascularization. However, stroke occurred significantly more often after CABG than after percutaneous coronary intervention (2.2% vs. 0.6%, p=0.003)(1). This discrepancy heightened awareness among the cardiology and cardiac surgical community regarding stroke after coronary artery bypass surgery and highlighted the need for further improvement in cardiac surgical techniques to reduce the incidence of this devastating surgical complication.

Stroke remains a significant cause of morbidity and mortality after coronary artery bypass grafting (CABG), occurring in approximately 1-14% of patients(2, 3). In addition, long-term survival of post-CABG stroke patients is negatively impacted with reductions in one- and five-year survival to 66 and 44% compared to 94 and 81% without stroke(4). The incremental cost of a postoperative stroke has been reported to be an additional $19,000 to the health system when there are no other associated complications and greater than $58,000 when combined with two or more other complications(5). The effect of stroke on ultimate patient recovery and quality of life is immeasurable since these patients frequently require prolonged supportive care at long-term rehabilitation units or acute-care facilities.

Patients undergoing CABG with ascending aortic atheromatous disease are known to carry increased risk of death, stroke, and major adverse cardiac events(4, 6, 7). With published reports indicating that up to 75% of all strokes following CABG are embolic and early (≤ 24 hrs postop) in nature(3), it is critical to make every effort to reduce the risk of distal embolization from aortic atheromatous disease. Several studies have confirmed the production of aortic emboli associated with the application of aortic clamps(8, 9, 10, 11, 12). Thus, the risk of atheroembolic stroke may be directly associated with aortic clamping which is commonly performed during CABG. The purpose of this study was to determine the impact of different aortic clamping strategies on the incidence of postoperative stroke.

BACKGROUND

Traditionally, CABG involves the use of autologous grafts which are used to bypass diseased coronary arteries. The left internal mammary artery is an in situ arterial graft which is almost always used to bypass the left anterior descending coronary artery, the artery responsible for blood supply to approximately 50% of the left ventricle. Saphenous vein grafts or other arterial grafts are used as free grafts to bypass other diseased coronary arteries. The distal ends of these grafts are anastomosed to the coronary artery while the proximal ends are typically sewn to the ascending aorta to provide inflow. The left internal mammary artery graft is performed in situ; thus no proximal aortocoronary anastomosis is necessary.

Furthermore, the majority of CABG cases in the United States are performed with cardiopulmonary bypass support. This involves cannulating the ascending aorta for arterial outflow and right atrial cannulation for venous inflow. To arrest the heart a clamp is placed over the entire circumference of the ascending aorta (cross-clamp) proximal to the aortic cannula. A potassium cardioplegia solution is then infused proximal to the cross-clamp which perfuses the heart and achieves cardiac arrest and provides for myocardial protection while the heart remains arrested. This enables the surgeon to perform distal anastomoses on a motionless and relatively bloodless field. After completion of the distal anastomoses, the surgeon has two options: 1) perform the proximal aortocoronary anastomoses with the heart arrested (under single cross-clamp, Figure 1) or 2) remove the cross-clamp to allow the heart to reperfuse and apply a partial-occluding clamp (occludes half the diameter of the aorta, Figure 2) to allow for proximal anastomoses to be constructed on an isolated segment of the ascending aorta while still allowing for myocardial perfusion around the partial-occluding clamp.

An alternative strategy for CABG involves performing the operation without the use of cardiopulmonary bypass, or off-pump. This obviates the need for aortic cannulation and aortic cross-clamping but typically still requires the placement of a partial-occluding clamp to perform aortocoronary proximal anastomoses. Alternatively, clampless facilitating devices are now available (Heartstring^{TM}, Maquet Cardiovascular LLC, San Jose, CA)(Figure 3) which allow for aortocoronary proximal anastomoses to be performed with minimal aortic manipulation. These devices can be applied to disease free portions of the aorta to minimize the risk of atheroembolism. Instead of clamping relatively large portions of the aorta, these devices punch a 4mm hole in the aorta and deliver a sealing cup to prevent blood loss during the proximal anastomosis which is later removed prior to tying down the suture. Finally, off-pump coronary artery bypass can also be performed without any aortic manipulation (no-touch). This can be accomplished by using in situ arterial grafts or by performing proximal anastomoses to in situ arterial grafts. By completely avoiding aortic manipulation, the risk of aortic atheroembolism is essentially eliminated.

Although a variety of methods exist for constructing proximal anastomoses, which method is associated with the lowest incidence of postoperative stroke is not well defined. Although postoperative stroke is believed to be strongly related to aortic manipulation during CABG, the etiology is most likely multifactorial. Although emboli during aortic manipulation may account for the majority of these events, other patient specific variables have also been implicated. These include pre-existing cerebrovascular disease, perioperative hypotension, atrial fibrillation, carotid disease, and diabetes mellitus. However, if mechanical factors such as operative techniques can be altered to minimize the risk of cerebral atheroembolism, then the incidence of this devastating complication can be reduced. Therefore, the purpose of this study was to determine which method was associated with the lowest incidence of postoperative stroke.

METHODS

The null hypothesis for this study was that strategies to reduce aortic manipulation did not reduce the incidence of postoperative stroke. This study was a retrospective, single center, case control study designed to evaluate the effect of different clamping strategies on the incidence of postoperative stroke. Emory University's Institutional Society of Thoracic Surgeons (STS) Adult Cardiac Database was queried for all patients (cases) with postoperative stroke after isolated, primary CABG. Controls were selected from the entire cohort without postoperative stroke. All consecutive patients from January 1, 2002 to December 31, 2009 were included in the database query. A case control study design was chosen because operative details about aortic clamping methods are not currently available in the STS database. Operative reports were reviewed and detailed data collected about whether patients underwent an on-pump or off-pump strategy, details about aortic clamping methods, and the extent of aortic atherosclerosis measured by epiaortic ultrasound (Figure 4). This data was then merged with the STS database to produce the complete dataset. Patients undergoing concomitant cardiac operations or those undergoing redosternotomy were excluded from this study because it is well accepted that these patients have a different risk profile. The STS database provides over 100 pre-, intra-, and postoperative variables about all patients undergoing cardiac surgery. Data is entered into the National STS database by trained data abstracter and is secured with passwords and firewall protection. Over 95% of all practicing adult cardiac surgeons participate in the National STS database. The study was approved by the Institutional Review Board at Emory University in compliance with HIPAA regulations and the Declaration of Helsinki. The Institutional Review Board waived the need for individual patient consent.

Matching algorithm

As part of the STS database, a predicted risk of postoperative stroke score (PROPS) is calculated based on 26 preoperative variables (Table 1) believed to be associated with increased risk of postoperative stroke. Controls were matched 4:1 to cases based on PROPS score as well as whether patients underwent CABG with cardiopulmonary bypass support (on-pump) or without cardiopulmonary bypass (off-pump). On- or off-pump was used in the matching algorithm because the goal of the study was to determine the impact of aortic clamping strategies or aortic manipulation on the incidence of postoperative stroke and not the effect of an on- or off-pump strategy. Therefore, on-pump cases were matched to on-pump controls and off-pump cases were matched to off-pump controls. An optimal matching algorithm was used which is designed to identify the best cutpoint for a continuous variable(13). The optimal matching algorithm is utilized as a SAS macro which defined a distance measure between cases and controls based on PROPS. The control chosen for each case is one that is closest to the case in terms of the distance measure produced by the matching algorithm. This algorithm sequentially matched each stroke patient with potential non-stroke controls by calculating the multivariate distance between the patients based on the 26 variables that comprise the PROPS score that were available preoperatively. The algorithm chooses the set of matches that minimizes the sum of the multivariate distances across all possible sets of matches.

Surgical Technique

For patients undergoing on-pump CABG, the most common clamping strategies in this study involved either a single cross-clamp or a double clamp technique. Other less commonly utilized on-pump strategies include an on-pump beating heart approach which obviates the need for an aortic cross-clamp. Proximal anastomoses can then be performed with a partial-occluding clamp or clampless facilitating devices.

For patients undergoing off-pump CABG, the most common methods for performing aortocoronary proximal anastomoses involve the use of a partial-occluding clamp or clampless facilitating devices. A less common strategy includes a "no-touch" technique in which proximal anastomoses are performed to in situ arterial grafts or in which in situ arterial grafts are utilized exclusively which obviates the need for proximal anastomoses. All surgeons in our center have a relatively uniform approach and extensive experience with on- or off-pump CABG.

Epiaortic Ultrasound

Epiaortic ultrasonography is now routinely used in all patients undergoing cardiac operations at Emory University. Its use was implemented in 2002 (coinciding with beginning of study period) and has become universally adopted for patients in which a clamp is being considered. Therefore, this non-invasive procedure is considered standard of care within our institution. Intraoperative epiaortic ultrasound has been shown to be superior to transesophageal echocardiography or palpation alone in identifying aortic atheromatous lesions(14, 15, 16) thus making it the modality of choice in identifying ascending aortic atheroma. Prior to aortic manipulation, the majority of patients currently undergo epiaortic ultrasonography to quantify the burden of atheromatous disease in the ascending aorta (Table 2). After screening, grade of aortic disease is determined according to thickness and the presence of mobile atheroma. The epiaortic grade was controlled for in the logistic regression analysis since patients with advanced aortic disease are believed to be at higher risk of atheroembolism related to aortic manipulation.

Outcome

The primary outcome was postoperative stroke which is defined as a new focal permanent neurological deficit on clinical exam which was diagnosed by an attending neurologist and confirmed with either brain computed tomography or magnetic resonance imaging. Stroke was differentiated from transient ischemic attack or postoperative delirium by clinical and radiologic exam.

Statistical Analysis

A conditional logistic regression analysis was performed to assess the association between the use of aortic clamping and postoperative stroke with adjusted odds ratios (AOR) and 95% confidence intervals (CI). This analysis was used to evaluate the effect of clamp versus no clamp controlling for matching factors (PROPS and pump) and epiaortic grade. Epiaortic grade was controlled for as both a 5-level ordinal and dichotomous variable in the regression analysis. Because epiaortic ultrasound use was not ubiquitous until recently, the analysis was also performed without controlling for epiaortic grade. In addition, conditional logistic regression analysis was used to evaluate the effect of different clamping or non-clamping strategies within on- and off-pump cases and controls. The initial model was designed to assess for the association of any clamping of the aorta on the incidence of postoperative stroke. In this model, potential preoperative confounding variables were controlled for by the matching algorithm for PROPS, the composite risk score which assigns an estimated risk score for the incidence of postoperative stroke based on 26 preoperative variables believed to be associated with risk of postoperative stroke. The effect of cardiopulmonary bypass, or on-pump, as a potential confounder was also controlled for in the matching strategy, since cases were matched separately to controls based on whether or not an on- or off-pump strategy was utilized. The influence of ascending aortic atherosclerosis, measured by epiaortic ultrasound, was controlled for in the analysis both as a continuous variable (epiaortic grade 1-5) as well as a dichotomous variable (low-grade 0-2, high-grade 3-5). To determine if the year of surgery confounded the analysis, year was also analyzed separately in modifications of the model.

Within each subset of operative strategy (on- or off-pump), separate models were developed to determine the association of different clamping strategies on the incidence of postoperative stroke, controlling for PROPS and epiaortic grade. Within the on-pump group, a double clamping strategy was compared to a single cross-clamp strategy. Within the off-pump group, a partial-clamping strategy was compared to a Heartstring only strategy and a partial-clamping strategy was compared to a no-clamp strategy (Heartstring or no-touch technique).

In addition to logistic regression analysis, descriptive analyses were performed to be able to assess trends in clamp use as well as trends in risk profiles and epiaortic use. All analyses were performed using SAS Version 9.2 (Cary, NC). All comparisons were made at the 0.05 alpha level.

RESULTS

Cases and controls were selected from a total cohort of 10,054 consecutive patients undergoing primary isolated CABG. From this cohort, there were 140 patients that suffered a postoperative stroke. Controls (565 patients without postoperative stroke) were selected from the remaining 9,912 patients without postoperative stroke. Of the 705 patients in this case control study, 181 (25.6%) did not have epiaortic ultrasound performed. Preoperative demographic data are listed in Table 3.

In 2002, 47/86 patients (54.6%) did not have epiaortic exam performed, compared to 7/66 (10.6%) in 2009. Epiaortic ultrasound grading was performed in 525 patients (74.4%): 75(14.3%) had Grade 3-5 and 450(85.7%) had Grade 1-2 aortic disease. In patients with Epiaortic Grades 3-5, a clampless technique was used in 59.5%, 83.3%, and 93.3% of cases, respectively. In patients with Epiaortic Grades 1-2, clampless techniques were used in 3.8% and 7.8%, respectively (Table 4). Trends in postoperative stroke by epiaortic grade are listed in Table 5. The use of any aortic clamping method decreased throughout the study period, from 84/86 (97.7%) patients in 2002 to 48/66 (72.7%) in 2009 (Table 6). The risk profile of patients according to PROPS score did not change over the course of the study period as depicted in Table 7.

The primary aim of this study was to determine the association of aortic clamping with the incidence of postoperative stroke after isolated coronary artery bypass surgery. Multiple logistic regression modeling was performed with the effect of cardiopulmonary bypass (pump), PROPS, and epiaortic grade controlled for in the model. When epiaortic grade was controlled for as an ordinal variable (grade 1-5) in a multiple logistic regression the odds ratio was estimated at 1.19 (95% CI 0.53-2.67). With epiaortic grade controlled for as a dichotomous variable (low-grade=grade 1-2, high-grade=grade 3-5), the odds ratio was 1.46 (95% CI 0.60-3.56). Because this excluded 181 patients in whom epiaortic ultrasound was not performed, the analysis was also performed without controlling for epiaortic grade to include all patients in the study. The estimated odds ratio for this analysis was 1.28 (95% CI 0.76-2.17).

Subgroup multiple logistic regression analysis was then performed according to surgery type (on- or off-pump) controlling for epiaortic grade to determine the association of various clamping and non-clamping strategies with the incidence of postoperative stroke. For patients undergoing on-pump coronary artery bypass with cardiac arrest, a two-clamp strategy (cross-clamp for cardiac arrest and distal anastomoses followed by a partial clamp for proximal anastomoses) was associated with a 2.5-fold increase in the incidence of postoperative stroke compared to a single clamp strategy (distal and proximal anastomoses performed under single cross-clamp)(adjusted odds ratio 2.60, 95%CI 1.03-6.67). For patients undergoing off-pump CABG, a partial clamp strategy versus the use of clampless facilitating devices (Heartstring) was associated with an adjusted odds ratio of 1.46 (95% CI 0.49-4.4). For patients undergoing off-pump CABG, a partial clamp strategy versus a no clamp strategy (Heartstring or no aortocoronary proximals) was associated with an adjusted odds ratio of 1.21 (95% CI 0.48-3.03). The effect of year of surgery was evaluated in all analyses and not found to be significantly associated with the incidence of postoperative stroke.

DISCUSSION

Stroke remains one of the major complications after CABG. In addition to aortic manipulation, advanced age, female sex, previous stroke, postoperative atrial fibrillation, carotid stenosis, hypertension, and diabetes mellitus have all been associated with increased risk of stroke after CABG(2, 3, 17, 18, 19, 20). As our understanding of the risk factors for stroke has increased, more attention is being focused on the observation that most strokes are embolic in nature and are discovered early after surgery (≤ 24 hrs postop). With published reports indicating that up to 75% of all strokes following CABG are embolic(3), it becomes critical to make every effort to reduce the risk of distal embolization from aortic atheromatous disease.

Manipulation of the aorta during CABG is still utilized for the following reasons: 1) placement of the aortic cannula for cardiopulmonary bypass; 2) cross-clamping to deliver cardioplegia and achieve cardiac arrest; 3) placement of a partial-occluding clamp to allow for coronary perfusion during performance of proximal arterial and/or venous anastomoses; 4) partial clamping to perform proximal anastomoses during OPCAB; and 5) performing proximal anastomoses without an aortic clamp using facilitating or anastomotic devices which minimize but do not eliminate aortic manipulation. During on-pump CABG, some surgeons prefer to use a cross-clamp for cardioplegic arrest, followed by removal of the cross-clamp and application of a partial-occluding clamp to perform proximal anastomoses. This reduces the ischemic time and allows for construction of proximal anastomoses during reperfusion. Most cerebral embolic events have been shown to occur at the time of clamp removal(21).

Studies utilizing transcranial Doppler ultrasonography have confirmed the production of aortic emboli associated with cannulation and application of aortic clamps(8, 9, 10, 11, 12). Bowles et al demonstrated large quantities of aortic emboli production during cardiopulmonary bypass without manipulation of the aorta utilizing transcranial Doppler ultrasonography (TCD)(22). Furthermore, Kapetanakis and colleagues(23) and Calafiore and associates(24) concluded that aortic manipulation is independently associated with an increased risk of postoperative stroke.

Epiaortic ultrasound has been used with increasing frequency by cardiac surgeons to assess the degree of atheromatous disease of the ascending aorta. It provides a simple, non-invasive, and inexpensive means to provide the surgeon with valuable information prior to aortic manipulation and enables surgeons to modify their technique based on the results. As shown in this study, epiaortic ultrasound use increased from approximately 50% in 2002 to approximately 90% in 2009. Current reasons for not performing epiaortic ultrasound include patients undergoing a single vessel off-pump CABG with an in situ arterial graft or patients undergoing double vessel off-pump CABG with 2 in situ arterial grafts. In these patients, there are no plans for any aortic manipulation and therefore this test is not performed. Similarly, for patients undergoing minimally-invasive CABG with a single in situ arterial graft, the aorta is not exposed and thus epiaortic ultrasound not performed.

Off-pump CABG eliminates the need for aortic cannulation, cardiopulmonary bypass, and application of a cross-clamp but does not eliminate the need for construction of proximal anastomoses in most cases. Specifically, when arterial or venous conduits still require the creation of proximal anastomoses, either a partial-occluding clamp is used or a facilitating or anastomotic device is usually used. Although complete avoidance can be performed with a "no touch" technique by sewing proximal anastomoses to *in situ* arterial grafts, this is not a common method for proximal anastomoses and is utilized as a last resort.

Previous work by Puskas and colleagues(25, 26) showed that the use of off-pump CABG versus on-pump CABG decreased the incidence of stroke. An intention-to-treat retrospective analysis of 42,477 patients from the Society of Thoracic Surgeons National Database showed a reduction in risk-adjusted operative mortality as well as a reduction in stroke favoring patients undergoing off-pump CABG(27). This study from our institution and others(26, 27, 28) have demonstrated that operative mortality and morbidity including stroke may be reduced in patients undergoing off-pump CABG compared to on-pump CABG.

A previous study evaluated the impact of a history of preoperative stroke on postoperative outcomes after CABG(17). The main findings were 1) that patients with a history of preoperative neurologic events had a significantly higher risk of suffering postoperative neurologic events, including permanent stroke and transient ischemic attack, and consequently had a higher in-hospital mortality rate, and 2) patients undergoing OPCAB were significantly less likely to develop postoperative neurologic events compared to patients undergoing on-pump coronary artery bypass.

In a study by Hannan et al(29), 49,830 patients from the New York state registry underwent risk-adjusted analysis (Cox proportional hazard models and propensity analysis) comparing outcomes after off-pump CABG vs. on-pump CABG. In this study, off-pump patients had significantly lower 30-day mortality, as well as a lower incidence of postoperative stroke. However, the mechanisms responsible for the observed reduction in postoperative stroke were not defined. Although off-pump avoids the use of cardiopulmonary bypass, postoperative stroke was not significantly reduced in two recent meta-analyses of off- versus on-pump CABG among relatively low risk patients(30, 31). Furthermore, partial aortic clamping (partial-occluding clamp) for construction of proximal anastomoses is still routinely performed in our center and by others for patients undergoing off-pump CABG. Thus, the benefits of off-pump CABG with regards to postoperative stroke may be attenuated because of the aortic manipulation and atheroembolic risk associated with partial aortic clamping commonly performed during off-pump CABG. Kim and associates reported a lower incidence of postoperative stroke in patients undergoing off-pump CABG without any manipulation of the aorta compared to patients undergoing off-pump CABG with partial clamping and patients undergoing on-pump CABG(32). Thus, the mechanism explaining why the incidence of postoperative stroke may be lower in patients undergoing off-pump CABG has not been well defined. Hammon and colleagues reported reduced neuropsychological deficits in patients undergoing on-pump CABG via single cross-clamp compared to patients undergoing on-pump CABG with multiple cross-clamping or patients undergoing off-pump CABG and partial clamping(33).

In the previous studies, little was known about the techniques used for construction of proximal anastomoses, and differences in the techniques used were not accounted for in the analyses performed. Avoiding partial clamping during construction of proximal anastomoses in OPCAB cases can be achieved by performing proximal anastomoses to *in situ* arterial grafts, or using proximal automated proximal anastomotic connectors or facilitating devices such as the Heartstring proximal anastomosis system, both of which can be performed without a partial aortic clamp. In a randomized clinical trial evaluating the PAS-Port proximal anastomotic connector versus construction of hand-sewn proximal anastomoses with partial clamping, all of the reported strokes occurred in patients in which an aortic clamp was used(34). In our preliminary experience, the Heartstring device was used to construct 647 clampless proximal coronary anastomoses during OPCAB. Among a total of 426 patients, only 3 patients (0.7%) suffered a postoperative stroke: 1 patient (0.5%) with minimal ascending aortic atherosclerosis (n=188), 1 patient (0.6%) with moderate ascending aortic atherosclerosis (n=177), and 1 patient (1.6%) with severe ascending aortic atherosclerosis (n=61). Although observational, this preliminary data suggests that minimizing aortic manipulation by avoiding an aortic clamp may be a valuable tool to reduce atheroembolic cerebral events.

In preliminary work at our institution, we randomized 57 OPCAB patients with mild ascending aortic disease to receive either partial clamping (n=28) or the Heartstring clampless device (n=29) for proximal graft construction on the ascending aorta. Continuous TCD monitoring was used intraoperatively to monitor embolic signals in the middle cerebral arteries, signifying embolic events. The number of embolic signals was significantly lower in the Heartstring group than in the partial-clamping group (50.8±36.6 vs.90.0±64.0; p=0.007)(35). Two delayed clinical strokes were observed in the clamping group and none observed in the clampless group, but the study was not powered to detect clinically significant events.

In this study, the primary goal was to determine the association of clamping strategies with the incidence on postoperative stroke. Unlike the previous aforementioned studies, the purpose was not to determine the association of an on- or off-pump strategy on stroke since this has previously been described. And although controversial, there is no clear consensus on the association between the use of cardiopulmonary bypass and the incidence of postoperative stroke. Therefore, this study focused on the association between aortic clamping and postoperative stroke. Both cardiopulmonary bypass use (pump strategy) and epiaortic grade were controlled for in the analysis since both are believed to play a role in the incidence of postoperative stroke. The main difference is that an on-pump strategy mandates at least some degree of aortic manipulation whereas a strategy of minimal manipulation is possible with an off-pump approach, either by having no manipulation or by using clampless facilitating devices.

In this study, the impact of any aortic clamping had only a modest effect on the incidence of postoperative stroke, which did not reach statistical significance. The result did not change when epiaortic grade was controlled for either as an ordinal or dichotomous variable, or was omitted from the analysis altogether. When evaluating the association of clamping strategies on postoperative stroke within each subgroup of surgery type (off- and on-pump), there was a significant association within the on-pump group. For patients undergoing a two clamp strategy versus a single cross-clamp approach, there was a 2.5-fold increase in the incidence of postoperative stroke, even after controlling for epiaortic grade. Within the off-pump cohort, there was a trend toward a higher risk of stroke for patients undergoing a partial clamping strategy versus a no-clamp strategy although these results did not reach statistical significance.

The interpretation of these results can be explained by several limitations. Although the case control design made data collection possible by limiting review of operative notes to 705 patients, the sample size may have been inadequate to detect statistically significant differences between the various clamping strategies. In order to have made this a cohort instead of a case-control study design, operative notes of over 10,000 patients would have required review. Because the overall incidence of postoperative stroke in this cohort was relatively low (<2%) detecting differences in clamping strategies is difficult. Furthermore, controlling for epiaortic grade may have further limited since this variable was incomplete and precluded analysis in patients that did not have epiaortic testing performed. Finally, as the descriptive analyses revealed, surgeon behavior changed over the time course of the study which may have introduced confounding into the study. Despite controlling for stroke risk using the matching variable PROPS and pump strategy and epiaortic grade, it is apparent that surgeons used clamping less frequently toward the end of the study period compared to the beginning of the study. Furthermore, surgeons were unlikely to use clamping methods in patients with high-grade aortas which may have minimized the effect of aortic clamping on the incidence of stroke since high grade aortas were rarely clamped. This change in approach likely reflects bias on the perceived risk of postoperative stroke associated with aortic clamping, especially in patients with advanced aortic disease determined by epiaortic ultrasound. Although the risk profile of patients did not change appreciably over the study period, the use of epiaortic ultrasound and clamping did. This reflects surgeons' beliefs that clamping high grade aortas is associated with higher atheroembolic stroke risk. The lack of increase in stroke according to epiaortic grade (Table 5) can be interpreted in two ways: 1) that epiaortic grade does not influence stroke or 2) that stroke incidence did not increase in higher grade aortas because of changes in strategy that occurred because of the epiaortic data available with this modality of testing.

Nonetheless, the results of this study do validate other studies in that patients undergoing on-pump CABG, which currently represents approximately 80% of cases in the US, have a lower risk of postoperative stroke when a single cross-clamp strategy is employed compared to a double clamp strategy. Whether these results can be used to claim that stroke risk is higher in off-pump patients undergoing clamping remains controversial. Future studies that examine different endpoints such as neurocognitive function or brain imaging which may be used as a better surrogate for brain injury than overt stroke may serve to identify the optimal strategy for minimizing adverse neurological outcomes after CABG.

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Table 1. Preoperative Variables Used to Calculate Predicted Risk of Postoperative Stroke

Variable
Age
Gender
Race
Ethnicity
Height (cm)
Weight (kg)
Diabetes
Last preoperative creatinine level
Dialysis-dependent renal failure
Hypertension
Infectious Endocarditis
Chronic lung disease
Immunosuppressive medication
Peripheral Vascular disease
Cerbrovascular disease
Pervious Cardiovascular Interventions
Preoperative Myocardial Infarction
Cardiac Presentation (urgent/emergent)
Preoperative Inotropes
Number of Diseased Vessels and Left Main

Stenosis >50%

Aortic Stenosis/ Insufficiency

Mitral Stenosis / Insufficiency

Tricuspid Insufficiency

Incidence (primary or redo)

Status

Preoperative Intra-aortic Balloon Pump

Table 2. Epiaortic Ultrasound Grading System Used at Emory University

Epiaortic Ultrasound Grade	**Intimal Thickness/Severity of Disease**
1	Normal (<2mm)
2	Mild (2-3mm)
3	Moderate (3-5mm)
4	Severe (>5mm)
5	Mobile Plaque, Any Thickness

Table 3. Preoperative Demographic Data

Variable	**Postoperative Stroke (N=140)**	**No Postoperative Stroke (N=565)**	**p value**
Age (mean ± SD)	65.7 ± 10.6	66.8 ± 10.3	0.65
Male (%)	82 (58.2)	353 (62.5)	0.35
Body Mass Index (mean ± SD)	29.0 ± 6.9	30.5 ± 23.0	<0.001
Preoperative Stroke (%)	33 (29.7)	103 (20.6)	0.04
Cerebrovascular Disease (%)	44 (31.2)	161 (28.6)	0.54
Hypertension(%)	127 (90.1)	504 (89.4)	0.81
Diabetes (%)	70 (49.7)	256 (45.4)	0.36
Renal Insufficiency (%)	16 (11.4)	57 (10.1)	0.67
History of Smoking (%)	59 (63.4)	330 (69.8)	0.23
Left Main disease (%)	35 (25.0)	187 (33.3)	0.06
Prior Myocardial Infarction (%)	50 (53.8)	260 (55.0)	0.83
Peripheral Vascular Disease (%)	34 (24.1)	109 (19.4)	0.21
PROPS score (mean % ± SD)	2.6 ± 2.2	2.6 ± 2.2	0.93

PROPS = predicted risk of postoperative stroke

Table 4. Trends in Epiaortic Ultrasound Use at Emory University Hospitals for Isolated Coronary Artery Bypass Surgery

Year	**Epiaortic ultrasound not performed**	**Total**	**%**
2002	47	86	54.7%
2003	30	71	42.3%
2004	28	98	28.6%
2005	28	109	25.7%
2006	19	102	18.6%
2007	16	100	16.0%
2008	6	74	8.1%
2009	7	66	10.6%

Table 5. Incidence of Postoperative Stroke According to Epiaortic Grade

Epiaortic Grade	**Controls (no postoperative stroke)**	**Cases (postoperative stroke)**
1	245 (77.8%)	70 (22.2%)
2	101 (78.9%)	27 (21.1%)
3	33 (78.6%)	9 (21.4%)
4	14 (77.8%)	4 (22.2%)
5	15 (100%)	0
Total	411	114

Table 6. Trends in Clamp Use by Year

Year	No Clamp (N=124)	Clamp (N=582)	Total
2002	2 (2.3%)	84 (97.7%)	86
2003	9 (12.7%)	62 (87.3%)	71
2004	13 (13.3%)	85 (86.7%)	98
2005	28 (25.7%)	81 (74.3%)	109
2006	20 (19.6%)	82 (80.4%)	102
2007	18 (18%)	82 (82%)	100
2008	16 (21.6%)	58 (78.4%)	74
2009	18 (27.3%)	48 (72.7%)	66

Table 7. Average PROPS score by year

Year	**Average PROPS score (%)**
2002	2.7
2003	2.5
2004	2.6
2005	2.8
2006	2.4
2007	3.1
2008	2.0
2009	2.5

PROPS = predicted risk of postoperative stroke

Figure 1. Aortic cross-clamp used to completely occlude the aorta

Figure 2. Aortic partial-occluding clamp which partially occludes the aorta to allow for coronary perfusion during proximal anastomoses.

Figure 3. Clampless facilitating device. The Heartstring device allows for proximal anastomoses to be performed without the use of a clamp.

Figure 4. Datasheets used to collect operative technical details about clamping techniques.

STROKE STUDY

Patient Name:___________________________

MRN:______________________________

Date of Surgery:___________________________

STROKE: Yes No

Timing of Stroke: ≤24 hours >24 hours

Incision:

Sternotomy: Yes No

Mini thoracotomy or thoracotomy: Yes No

Epiaortic ultrasound done? Yes No

Epiaortic Grade: I II III IV V

Cardiopulmonary bypass utilization:

Off-pump: Yes No

Converted to on-pump: Yes No

Emergently: Yes No

On-pump:

On-pump cardioplegic arrest (cross-clamp): Yes No

On-pump beating heart (no cross clamp): Yes No

On-pump fibrillatory arrest (no cross-clamp): Yes No

Method of Arterial Cannulation: Aortic Femoral Axillary

Method of Proximal Anastomosis:

Single cross-clamp (on bypass, cardioplegic arrest): Yes No

Needed re-cross-clamp and re-arrest: Yes No

Partial clamp (side-biting clamp): Yes No

Heartstring Proximal or Pas-Port: Yes No

Number of Heartstring Proximals done: 1 2 3 4

Heartstrings and partial clamp done: Yes No

No touch aortic technique (no aortic proximals): Yes No

Partial occluding clamp applied more than once: Yes No

Proximals taken off of LIMA: Yes No

Comments:____

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Read by:

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