

## "AWAKE" TRANSAPICAL AORTIC VALVE IMPLANTATION-EARLY EXPERIENCE.

Mukherjee D; Walther T; Borger M; Falk V; Mohr F; Ender J

*Heartcenter Leipzig, University Leipzig*

### Purpose:

Transapical aortic valve implantation (TA AVI) is a new technique for beating heart off-pump therapy in high risk patients with symptomatic aortic stenosis.(1).Our standard protocol in these patients is general anesthesia with early extubation,using fast track anesthesia (2).We have performed these procedure in 7 high risk patients who underwent TA AVI awake,using thoracic epidural anesthesia.

### Methods:

Patient selection was performed on the basis of an increased perioperative risk profile according to the Euro score scale .All these patients had a FEV1 < 60% of predicted value in lung function test, with other associated co-morbidities.The epidural catheter was placed in T2-T3 region using the LOR and hanging drop technique. Ropivacaine 0.2% was administered as test dose (x ml) and followed with continuous infusion of ropivacaine and fentanyl.Motor blocked achieved till T 10 and sensory blockade till T12. After the pleura was opened, lung collapse was avoided and saturation was maintained using CPAP mask with a pressure of 10mbar. Patients did not experience any pain and discomfort during the procedure. Communication was maintained throughout the surgery using head movements from the patient. Post operative analgesia was delivered for 4 days through the catheter which was then removed after the coagulation profile was normalised.

### Results :

2 Patients were converted to general anesthesia.One patient had to be converted owing to surgical reasons(sternotomy and extracorporeal circulation) and the second patient did not want to be awake. Rest 5 patients had an uneventful and satisfactory outcome.These patients had a VAS score of 1 post operatively. They did not experience any untoward side effects of ropivacaine. As the patients were awake throughout the procedure and received CPAP ventilation ,they did not require any intubation.As the results were satisfying and pain scores were minimal,they could be discharged on the 10th post-operative day.

### Conclusion:

Our early experience shows that awake TA AVI is feasible in these high-risk patients ,particularly those with underlying pulmonary disease. We have performed 7 "awake" TA AVIs in our institute with satisfactory outcome,although further evaluation in larger number of patients will be required.

### Reference:

1. Walther T,Falk V, Borger MA,Dewey T,Wimmer-Grienecker G,Schuler G,Mack M,Mohr FW: Minimally invasive transapical beating heart aortic valve implantation: Proof of Concept: European Jour. Cardiothoracic Surg: 2007 -31 (9-15)
2. Ender J, Borger MA, Scholz M, Funkat AK, Anwar N, Sommer M, Mohr FW, Fassl J. Anesthesiology. 2008 Jul;109(1):61-6.Cardiac surgery fast-track treatment in a postanesthetic care unit: six-month results of the Leipzig fast-track concept.

## 3D TRANSESOPHAGEAL ECHOCARDIOGRAPHY: DEVELOPMENT OF AN INTRAOPERATIVE CARDIAC SURGERY PROTOCOL

Purgess J; Gogoladze G; Grossi E

*New York Veterans Administration Hospital*

**Background:** Three dimensional transesophageal echocardiography (3D TEE) is emerging as an important diagnostic tool for cardiac surgery as well as an aid while performing intraoperative procedures. We have evaluated the utility of 3D TEE in the management of patients undergoing cardiac surgery, using that experience to develop a general protocol for such patients. While such protocols exist for 2D echocardiography (1), we are unaware of previously published guidelines for 3D TEE during cardiac surgery

**Methods:** We evaluated 61 patients for heart surgery with 3D TEE using multiple acquisition modes and angles in developing the protocol for subsequent patients. Images were obtained utilizing the iE33 Ultrasound System (Philips) with the X7-2t, a fully-sampled matrix array TEE transducer with ~2500 elements after performance of standard 2D echocardiography. We utilized the 4 available 3D acquisition modes: two which use real-time images (live 3D and live 3D zoom) and two which use reconstructed images (full-volume and 3D color Doppler). After first optimizing the 2D image, the 3D images were optimized using the density, FV Opt, XRes, gain, threshold and brightness controls. Live 3D images were cropped as appropriate.

We established the following for the Cardiac Surgery Intraoperative 3D TEE Protocol. 1) Full Volume image acquisition pre and post heart surgery through the mitral valve (mid-esophageal 4 chamber at 0°) for analysis of ejection fraction, 17 segment wall motion analysis and mitral valve quantification with QLab software (Philips); 2) 3D Color Doppler for valves with flow disturbances; 3) live 3D Zoom with image capture using the orthogonal views for the mitral and aortic valves (mid esophageal long axis view at ~ 120°); 4) tricuspid valve (mid esophageal RV inflow-outflow at ~ 60°) ; 5) intraatrial septum using Full Volume acquisition (mid esophageal four chamber at ~ 0°); 6) left atrial appendage (mid esophageal two chamber at ~90°); and 7) the aorta during pullback. These views should be acquired and archived. Live 3D is utilized for procedures (Swan-Ganz catheter passage/cannulation of the coronary sinus).

**Results:** Systematic use of this comprehensive 3D TEE protocol exam standardizes the acquisition of datasets for both intraoperative use as well as for later review using software tools (QLab). It serves as a baseline which can be modified during surgery according to the clinical situation, allows acquisition of all relevant information and facilitates development of technical skills. The data also serves as a clinical baseline for future evaluation of these patients.

**Conclusions:** 3D echocardiography is a technological advance with its potential yet to be fully realized. The establishment of a protocol provides a framework facilitating the use of intracardiac 3D TEE and ensures the gathering of essential information.

1. Shanewise JS et al: ASE/SCA guidelines for performing a comprehensive intraoperative multiplane transesophageal echocardiography examination. J Am Soc Echocardiogr 12:884-900, 1999.

## ABO BLOOD GROUP, TRANSFUSION AND MORTALITY AFTER CARDIAC SURGERY

Welsby I; Phillips-Bute B; Mathew J; Becker R; Stafford-Smith M

### *DUMC*

#### Background :

We have previously reported genetic associations with outcome after cardiac surgery. [1,2] ABO blood group is the most widely tested phenotype, and levels of the prohemostatic protein von Willebrand factor (vWf) differ depending on ABO blood with group O being the lowest and group AB the highest. Therefore, we tested the primary hypothesis that perioperative blood transfusion differs among blood groups and the secondary hypothesis that mortality will follow transfusion patterns.

#### Methods :

We evaluated 10,276 consecutive, non-emergent on-pump CABG and CABG/valve patients operated on at Duke Heart Center between June 1992 and March 2007. All patients undergoing coronary revascularization are followed up by the Duke Clinical Research Institute until death or lost to follow-up. Transfusion of packed red blood cells (PRBCs) over POD 0,1 and 2 was compared by Wilcoxon Rank tests for multiple groups and a Cox proportional hazards model compared survival; a Kaplan-Meier plot was constructed.

#### Results :

Blood types were retrieved for 9831 patients. Transfusion of PRBCs was lower for group AB (3[1-4] Vs 3[1-5];  $p=0.003$ ), therefore survival was evaluated for AB versus the remainder (O, A and B groups); the rate of CABG/valve surgery across groups was similar (10.7% AB Vs 11.2% other;  $p=0.78$ ). As illustrated in the Figure, group AB had better long-term survival ( $p=0.04$ ) in an unadjusted analysis. Adjusting for the number of PRBC units transfused, the Euroscore and CABG/valve procedure showed a trend in favor of group AB ( $p=0.08$ ) and this trend persisted in CABG only patients ( $p=0.08$ ).

#### Discussion :

We observed blood group dependent transfusion and long-term survival differences after coronary revascularization surgery. Group AB patients were transfused fewer PRBCs and had improved outcome compared to other groups. This observation can only be partly explained by PRBC transfusion and future mechanistic study targeting vWf profiles may explain our observation.

#### References :

1. Welsby et al. J Thromb Haemost. 2005; 3:1206-1213.
2. Podgoreanu et al. Circulation.2006;114:275.

## ANESTHETIC FACTORS AND THE RISK OF RESPIRATORY COMPLICATIONS AFTER PNEUMONECTOMY

Blank R; Scalzo D; Jones D; Gurka K; Jaeger J

*University of Virginia*

Although pneumonectomy is associated with the risk of serious complications and mortality (1,2), anesthetic factors contributing to increased risk have not been completely elucidated. Previous studies have implicated ventilatory factors such as tidal volumes and ventilatory pressures (3,4) as well as fluid intake (3,4) in the etiology of acute lung injury and respiratory failure, but the role of intraoperative and anesthetic factors remains incompletely understood.

To assess the effects of anesthetic factors on respiratory complications after pneumonectomy, we retrospectively examined the charts of 129 patients who underwent elective pneumonectomy at the University of Virginia between 1997 and 2008. Exposures included duration of anesthesia, ventilatory factors, fluid intake, vasopressor infusions, thoracic epidural analgesia, and intraoperative hypo- and hypertension. Respiratory failure (mechanical ventilation > 48 hr. postoperatively or the re-initiation of mechanical ventilation) and a composite of all respiratory complications (respiratory failure, air leak, atelectasis, pneumonia, bronchopleural fistula, pulmonary embolus, acute lung injury, ARDS) were the outcomes. Potential confounders included patient characteristics, comorbidities, pulmonary function tests, and surgical factors. Odds ratios were estimated with logistic regression and exact methods were used for small sample sizes.

The incidence of respiratory failure in this series was 13.2%; the incidence of acute lung injury and ARDS was 0.8% and 6.2%, respectively. Univariate analysis suggested significant associations between anesthetic factors and respiratory complications. Duration of anesthesia and respiratory complications were associated ( $p=0.03$ ) but the largest tidal volumes during one and two lung ventilation were not associated with respiratory complications. ASA status was associated with increased risk of respiratory failure ( $p<0.01$ ) and composite respiratory complications ( $p<0.01$ ). Although other covariates were associated with these outcomes, none appreciably confounded the exposure-outcome associations. Controlling for ASA status, single unit transfusion of packed RBCs significantly increased the risk of respiratory failure (OR=1.44, exact 95% CI: 1.02, 2.09), as did single unit transfusion of fresh frozen plasma (OR=3.57, exact 95% CI: 1.28, 24.11). Respiratory complications were also significantly associated with single unit transfusion of packed RBCs (OR=1.64, 95% CI: 1.15, 2.34) and one liter administration of crystalloid (OR=1.52, 95% CI: 1.02, 2.26) and total fluids (OR=1.46, 95% CI: 1.05, 2.04).

These findings support the concept that intraoperative and anesthetic factors, particularly the administration of blood products and fluid balance may have profound effects on respiratory function and the development of respiratory complications after pneumonectomy.

- 1) Bernard, A, Deschamps, C, Allen, MS et al. J Thorac Cardiovasc Surg 2001; 121:1076-1082
- 2) Harpole DH, Decamp, MM, Daley J et al. J Thorac Cardiovasc Surg 1999; 117:969-979.
- 3) Licker, M, de Perrot, M, Spiliopoulos, A et al. Anesth Analg 2003;97:1558-65.
- 4) Fernandez-Perez, ER, Keegan, MT, Brown, DR et al. Anesthesiology 2006; 105:2-5.

## APROTININ VERSUS TRANEXAMIC ACID IN LUNG TRANSPLANTATION

SUBRAMANIAM K; MARQUEZ J; SULLIVAN E

*UPMC*

**Background;** Aprotinin was used in all high risk cardiac surgery for hemostasis including lung transplant surgery requiring cardiopulmonary bypass. After aprotinin has been withdrawn from the market, tranexamic acid is being used in our institute as the antifibrinolytic. We reviewed the records for safety and efficacy of tranexamic acid compared to Aprotinin in lung transplant surgery

**Methods;** After permission from institutional review board, we reviewed the records of all lung transplants from May 2007 till June 2008. We obtained the demographic data, intraoperative variables (surgical and anesthetic), transfusion and reexploration in both the groups and various organ outcomes (death, respiratory, cardiac, renal and sepsis). All data were compared using appropriate statistical tests (SPSS 16.0) and  $P < 0.05$  was considered significant

**Results;** Of 98 records reviewed, 32 patients required cardiopulmonary bypass. Aprotinin was used in 18 patients and TA in 14 patients. Demographic data and intraoperative variables were similar. Chest tube drainage was similar. Mean packed red cell transfusion was  $3.44 \pm 2.83$  in aprotinin group versus  $3.64 \pm 2.87$  in TA group ( $P = 0.84$ ). Mean fresh frozen plasma and platelet transfusion was also similar in both groups. Two patients in aprotinin group and one in TA required re-exploration. Respiratory failure (ventilation > 48 hours) occurred in 9 patients in aprotinin and 9 patients in TA group ( $P=0.48$ ). Renal failure (>25% increase in CrCl) occurred in 7 patients in aprotinin and 8 patients in TA group ( $P=0.50$ ). Sepsis, stroke, atrial fibrillation, hospital and ICU stay were similar. TA group had more patients with altered mental status ( 8 patients in TA versus none in aprotinin  $P= 0.0003$ ).

**Conclusion;** TA was as effective as Aprotinin in reducing blood loss and transfusions in patients undergoing lung transplants. Adverse events were similar except postoperative altered mental status was higher in TA which requires further investigation

## ASSOCIATION OF POSTOPERATIVE HYPOALBUMINEMIA AND OUTCOME IN OFF PUMP CORONARY ARTERY BYPASS SURGERY

Choi D; Chin J; Lee E; Choi I

*Asan Medical Center*

**Background:** Decreases in serum albumin is commonly seen after surgery but the clinical relevance of postoperative hypoalbuminemia is less clear. The aim of the present study was to evaluate the relationship between the immediate postoperative serum albumin concentration and postoperative outcomes of patients undergoing off pump coronary artery graft (OPCAB) surgery.

**Methods:** We retrospectively analyzed 690 patients undergoing elective OPCAB surgery between January 1, 2006 and June 30, 2008. The lowest serum albumin level measured over the first 12 hours postoperatively was used to evaluate the role of albumin as a predictor of clinical outcome. Logistic regression analysis was performed to calculate the odds of morbidity and mortality according to the immediate postoperative serum albumin level.

**Results:** Immediate postoperative serum albumin concentration was independently associated with postoperative respiratory tract infection (odds ratio [OR], 0.09; 95% confidence interval [CI], 0.02 to 0.56; P=0.009), adult respiratory distress syndrome (OR, 0.07; 95% CI, 0.01 to 0.86; P=0.038), heart failure (OR, 0.03; 95% CI, 0.01 to 0.44; P=0.012), renal failure (OR, 0.19; 95% CI, 0.05 to 0.82; P=0.025), reoperation for bleeding (OR, 0.23; 95% CI, 0.06 to 0.92; P=0.037), GI complication (OR, 0.26; 95% CI, 0.08 to 0.91; P=0.034), longer extubation time (OR, 0.55; 95% CI, 0.34 to 0.89; P=0.015) and ICU stay (OR, 0.51; 95% CI, 0.32 to 0.81; P=0.005), the need for use of inotropes in ICU (OR, 0.55; 95% CI, 0.31 to 0.99; P=0.05), and in-hospital mortality (OR, 0.08; 95% CI, 0.01 to 0.91; P=0.041). However, it was not associated with arrhythmia, infective or neurologic complication, or length of hospital stay (P>0.05).

**Conclusions:** Low immediate postoperative serum albumin concentration is associated with poor postoperative outcomes in patients undergoing OPCAB. It may be used as a prognostic tool to detect the risk of adverse surgical outcomes.

## AUTOLOGOUS PLATELET RICH PLASMA TRANSFUSION REDUCES BLOOD PRODUCT REQUIREMENTS IN ASCENDING AORTIC ANEURYSM REPAIR WITH PROFOUND HYPOTHERMIA

Zhou S; Sheinbaum R

*The University of Texas Medical School at Houston*

SF Zhou;AL. Estrera;C Ignacio;S Panthayi;H Safi;C Miller;R Sheinbaum. INTRODUCTION: Coagulopathy is a common complication following Ascending Aortic Aneurysm (AcsAA) repair with deep hypothermic circuit arrest (DHCA). Platelet and factor dysfunction are major etiologies for intra and peri-operative bleeding, necessitating transfusion of blood products. Adverse outcome in cardiac surgery is associated with increased blood transfusions<sup>1</sup>. Utilization of autologous platelet rich plasma (PRP) in AscAA repair with DHCA is an effective, safe and simple process to improve hemostasis by preserving platelet and factor function. PRP results in significant reduction of intra and peri-operative transfusions.

MATERIALS AND METHODS: We retrospectively reviewed 363 cases of AscAA repair from Oct,2003-July,2008. 147 patients received PRP harvest and 216 patients did not. PRP was collected by harvesting 15-20 ml/kg whole blood prior to CPB and fractionating off the PRP component. The goal was a yield of 10 ml/kg of PRP. Statistical analysis of variance factors; Mean and the standard deviation were calculated for each variable. A P- value of less than 0.05 was considered significant. Fishers Exact Test was performed to assess changes and its relationship with postoperative complications.

RESULTS AND DISCUSSION: Demographics and surgical characteristics (excepting age) were similar between groups (Table 1). Intra-OP blood transfusions (Table 2, Fig. 1) were significantly reduced in the PRP cohort. The PRP group averaged 3.7 units less transfusion of PRBC, 4 units less of FFP, 7.5 units less of Platelets, and 4 units less of cryoprecipitate than the Non-PRP group. In the PRP group 29/147 (20%) received no transfusions and 31 /147 (21%) required 4 or less units of PRBC only. Postoperative homeostasis and hematocrit were similar between the two groups (Table 3).

CONCLUSION: Use of PRP in Ascending Aortic Aneurysm repair with deep hypothermic arrest results in improved hemostasis and reduced blood product transfusions. Reference: 1. Indications for blood transfusion in cardiac surgery. *Ann Thorac Surg.* 2006;82:2323-34. 2. A comparative study of the effect of autologous platelet-rich plasma and fresh autologous whole blood on hemostasis after cardiac surgery. *Cardiovasc Surg.* 1996 Feb;4(1):9-14.

## CAN CARDIAC ANESTHESIOLOGIST IMPACT ON THE OUTCOMES OF CARDIAC SURGERY?

Seino Y; Tomita Y; Iwata S; Onuki E; Shoji S; Kotani T; Nomura M; Ozaki M

*Tokyo Women's Medical University*

### Backgrounds:

The impact of cardiac anesthesiologists in postoperative care of cardiac surgical patients on outcomes is not fully defined<sup>1</sup>. The purpose of this retrospective study was to investigate the contribution of cardiac anesthesiologist in the postoperative care to cardiac patients' outcome.

### Methods:

We studied 149 consecutive cardiac surgical patients operated between January 2004 and June 2004 and managed by cardiac surgeons in postoperative care (group S), and 132 consecutive patients operated between January 2007 and June 2007 and managed by cardiac surgeons and cardiac anesthesiologists (group A).

28 day mortality, duration of mechanical ventilation, intensive care unit length of stay (ICU LOS), hospital length of stay (hospital LOS), rate of early extubation (<math>\leq 8\text{ h}</math>) and incidence of postoperative complication were compared between groups. Furthermore, these values were also compared in the high risk patients (EuroScore <math>\geq 6</math>) of both groups.

Statistical analysis was performed with unpaired t test, Mann-Whitney U test and Fisher's exact test. A p value of <math>< 0.05</math> was considered statistically significant. All values are shown as mean  $\pm$  standard deviation.

### Results:

Group demographics were comparable, except the proportion of high risk patients was higher in group S compared to group A (52.4% vs. 43.2%). PaO<sub>2</sub> /FiO<sub>2</sub> ratio and cardiac index on admission to the ICU were significantly higher in group A (325.2  $\pm$  121.4 vs. 390.4  $\pm$  121.7 torr and 3.1  $\pm$  0.9 vs. 3.6  $\pm$  1.2 L/min/m<sup>2</sup>, respectively). Hematocrit was significantly lower in group A (34.2  $\pm$  4.5% vs. 31.4  $\pm$  3.7%).

28-day mortalities were similar in both groups (1.3% group S vs. 2.3% group A). The ICU LOS (103.8  $\pm$  130.1 vs. 91.7  $\pm$  115.0 h) and hospital LOS (31.8  $\pm$  28.7 vs. 30.2  $\pm$  30.4 d) were significantly shorter in group A. Duration of mechanical ventilation was shorter in group A (34.3  $\pm$  78.3 vs. 28.0  $\pm$  43.6 h). The rate of early extubation (<math>\leq 8\text{ h}</math>) is significantly higher in group A (24.8% vs. 38.6%). The incidences of mediastinitis, surgical site infection and elevation of hepatic enzymes were significantly lower in group A (9.4% vs. 1.5% and 61.7% vs. 20.4% respectively). In the high risk patients, group demographics were also comparable. 28-day mortalities were similar in both groups (2.6% n=78 vs. 1.8% n=57). The hospital LOS was significantly shorter in group A (39.0  $\pm$  37.2 vs. 30.2  $\pm$  27.0 d). The ICU LOS (136.3  $\pm$  170.9 vs. 128.2  $\pm$  161.0 h) and duration of mechanical ventilation (49.7  $\pm$  103.0 vs. 42.0  $\pm$  58.8 h) were shorter in the group A. The rate of early extubation (<math>\leq 8\text{ h}</math>) was also significantly higher in group A (6.4% vs. 26.3 %).

### Conclusions:

Cardiac anesthesiologists can improve the outcomes of cardiac surgical patients by participating in postoperative care.

The duration of mechanical ventilation, the ICU LOS and hospital LOS are shortened and the rate of early extubation is increased in various risk patients.

The incidence of postoperative complication is also decreased.

### Reference:

1. Novick RJ, Fox SA, Stitt L, et al. Impact of opening of a specialized cardiac surgery recovery unit on postoperative outcomes in an academic health sciences center. *Can J Anesth* 2007;54:737-43

## CAN ECHOCARDIOGRAPHY PREDICT ATRIAL FIBRILLATION AFTER THORACIC SURGERY?

Semenya A; Amar D; Roistacher N; Zhang H

*Memorial Sloan Kettering Cancer Center*

**Background:** New onset postoperative atrial fibrillation (POAF) is a known marker of greater morbidity in patients having thoracic surgery. The purpose of this study was to measure echocardiographic indices of atrial function to try and predict which patients are at greater risk for POAF.

**Methods:** Using an ongoing prospective database, a subset of 83 patients who had a perioperative transthoracic echocardiogram (TTE) were identified. POAF was detected using continuous telemetry or 12-lead ECG. Patients were grouped based on whether they had a minor or major thoracic procedure and baseline characteristics were recorded (Table 1). TTE was used to determine left atrial volume (LAV), left ventricular diastolic function, estimated right atrial pressure (RAP), and systolic pulmonary artery pressure. LAV was estimated using Simpson's rule where  $LAV = 0.85 * [(Area\ of\ 4\ chamber\ view) * (Area\ of\ 2\ chamber\ view)] / (Length)$ . The length used was the shortest distance from the mitral valve to the superior LA wall in either view as per ASE guidelines. LAV was indexed by divided by Body Surface Area (BSA).

**Results:** Patients undergoing major surgery were older than those having minor surgery,  $p=0.02$  but did not differ in other characteristics, Table 1. POAF occurred in 12/50 (24%) major vs. 1/33 (3%) minor surgery patients,  $p=0.01$ . Among the major surgery group ( $n=50$ ) LAV and diastolic function did not differ between patients with or without POAF (Table 2).

**Conclusions:** POAF is a common complication of older patients having major thoracic surgery. Unlike studies in cardiac surgery patients, these preliminary data show that LAV and diastolic function variables did not predict those who did or did not develop POAF. Further study with a larger sample size is needed.

**References:** 1) Ann Thorac Surg 1996;61:516-20.

2) Chest 1995;108:349-54.

3) J Am Soc Echocardio 2005;18:1440-1463

## CAN WE REVERSE CLOPIDOGREL-INDUCED PLATELET DYSFUNCTION?

Rumph B; Szlam F; Bolliger D; Tanaka K; Levy J

*Emory University*

**Background:** Clopidogrel (Plavix, Sanofi-Aventis) is an irreversible P2Y<sub>12</sub> platelet receptor inhibitor crucial to platelet activation and thrombin generation. Therapy with clopidogrel is associated with increased bleeding risk with no known reversal agents. Recombinant human Factor VIIa (rFVIIa, Novoseven®, Novo Nordisk) has been shown to reverse coagulopathic bleeding due to platelet dysfunction. Therefore, we evaluated the effects of rFVIIa on thrombin generation in platelet rich plasma (PRP) from patients on clopidogrel therapy.

**Methods:** Following IRB approval, blood samples from 6 consented patients undergoing coronary interventions were drawn at baseline and 18-20 hours after a 600 mg loading dose of clopidogrel into 3.2% citrate tubes with 100 µg/ml corn trypsin inhibitor, then centrifuged at 150g for 5 min to obtain PRP. Platelet counts were adjusted to  $200 \times 10^9$  /µl with plasma obtained from the same sample, and aggregometry was performed with 2.0 and 20 µM ADP. For thrombin generation studies, 0.1 U of heparin was added to PRP samples which were then divided into 4 groups; (1)PRP only, (2)PRP+20 µM ADP, (3) PRP+20 µM ADP +60nM rFVIIa, and (4)PRP+60 nM rFVIIa. Modified Thrombin generation using Thrombinoscope technology was performed as described by Hemker [1], and lag time and peak thrombin generation were measured.

**Results:** Platelet aggregation decreased post-clopidogrel by an average of  $22.6 \pm 35.6\%$ , then platelets disaggregated. Time for thrombin generation (lag time) was significantly increased in post-clopidogrel samples compared to similar pre-clopidogrel samples in groups 2, 3, and 4. Combination of 60 nM rFVIIa and ADP was most efficacious in decreasing the lag time ( $70.1 \pm 6.4\%$ ) followed by rFVIIa alone ( $59.8 \pm 4.8\%$ ). The addition of rFVIIa to PRP improved lag time as much in post-clopidogrel samples as in pre-clopidogrel samples (there was no difference in effect of VIIa pre and post clopidogrel). Peak thrombin generation was similar in pre and post-clopidogrel samples.

**Conclusion:** Clopidogrel-treated platelets aggregate in response to ADP for a limited duration, then lose their ability to bind to fibrinogen (disaggregation). Heparin at 0.1 U/ml delayed the onset of thrombin generation after clopidogrel treatment. The addition of either high-dose ADP or rFVIIa improved the rate of thrombin generation. The maximal effects of rFVIIa were observed when platelets were also activated by ADP. This data indicates that platelets responded only to high doses of ADP, and rFVIIa appears effective in restoring hemostatic function following clopidogrel.

**References:** [1] Hemker, HC *Thromb Haemost*, 2000;84:747

## CARDIAC OUTPUT MEASUREMENT-USING FLOTRAC IN OFF-PUMP CABG: RADIAL ARTERY VS. FEMORAL ARTERY

Kanchi M; Aggarwal V

*Narayana Hrudayalaya*

### Introduction:

Haemodynamic assessment involving cardiac output measurement is of particular importance in patients undergoing off-pump coronary artery bypass grafting (CABG). Traditional thermodilution technique using a pulmonary artery catheter may not provide accurate information when heart is positioned for grafting in an off-pump scenario. The floTrac system provides cardiac output determination based on arterial pressure waveform any standard arterial catheter. However, the arterial pressure measured from radial artery may differ from that measured for femoral artery due to difference in the characteristics of the arterial wall in these two locations. Hence, this study was performed to determine whether cardiac output measured using a floTrac from radial artery correlates with that of femoral artery in off pump CABG.

### Methods:

After obtaining IRB and ethical approval, this study was conducted on 15 consecutive patients undergoing elective off-pump CABG. Catheters in radial and femoral artery were inserted under local analgesia and were connected to floTrac and arterial pressure was transduced. Anaesthesia was induced using standard technique of fentanyl, midazolam and endotracheal intubation was performed after pancuronium. The cardiac output, cardiac index, stroke volume variation, stroke volume/ index were derived from Vigelio monitor at specific time intervals. The data were statistically analyzed.

### Results:

Table-1 shows the means values of the haemodynamic variables in two arterial systems. Though the radial artery systolic pressure was higher than femoral, there were no differences in any other parameter at any point of measurement.

### Discussion:

Out study demonstrate that either of the sites of arterial pressure monitoring & CO measurements using floTrac provide similar data in patients undergoing off-pump CABG.

## CARDIOVASCULAR FELLOWSHIP TRAINING PROGRAMS: A SURVEY OF HOUSESTAFF SUPERVISION.

Soong W; Sherwani S

*Northwestern University*

**Introduction:** Fellowship education in Adult Cardiothoracic Anesthesiology was first recognized by the Accreditation Council for Graduate Medical Education (ACGME) in 2006. ACGME Program Requirements for anesthesiology residency training state, "In the clinical setting, faculty members should not direct anesthesia at more than two anesthetizing locations simultaneously." In contrast, Program Requirements for cardiothoracic fellowship training merely mandate "...adequate supervision of fellows at all times." In the process of realigning our practice model with the clinical and educational goals of our residency and fellowship programs, we conducted a survey regarding staffing of cardiac cases.

**Methods:** In May and November 2008, email invitations to participate in an online survey were sent to Program Directors at all cardiovascular anesthesia fellowship programs listed on the SCA website. Programs based at pediatric hospitals were excluded, as were those without a posted email address. The survey focused on clinical volume and attending physician coverage of housestaff during cardiac cases.

**Results:** Eighty fellowship programs were listed on the SCA website. Three pediatric programs were excluded, as were 20 other programs with either an invalid or no email address posted. Of the 57 remaining programs, 23 (40.5%) responded. There was a broad range in both annual and daily clinical volume (Table 1). Seven respondents (30.4%) indicated that attending anesthesiologists at their respective institutions simultaneously supervise two operating rooms (ORs). Respondents work primarily with CA-2s, CA-3s, and fellows in cardiac cases (Table 2). Rarely do fellows function in the capacity of supervising two resident ORs.

**Discussion:** Scant data address optimal coverage for the unique complexity and demands of cardiovascular anesthesia. One study failed to find a significant correlation between supervision of multiple cardiac anesthetics and perioperative morbidity and mortality. However, the majority of respondents to our survey indicated that their institutional practice is to single-cover cardiac ORs. In addition to patient safety, resident and fellow education must be taken into consideration. An observational study noted a 33% decrease in teaching when the attending anesthesiologist was involved in two concurrent cases. Although by no means a comprehensive analysis, our survey brings to question the appropriate supervisory ratio for cardiac cases, particularly when a fellow is involved. Further study is needed to determine the optimal practice model that balances patient safety, housestaff education, and medical economics.

## CEREBRAL UPREGULATION OF LIPOCALIN-2 FOLLOWING EXPERIMENTAL DEEP HYPOTHERMIC CIRCULATORY ARREST

Mackensen G; Ma Q; Podgoreanu M; Zhang Z

*Duke University Medical Center*

**Introduction:** Despite recent advances in thoracic aortic surgery, perioperative cerebral injury remains as a significant cause of associated morbidity and mortality. Perioperative cerebral injury has been linked to both, the cerebral ischemia-reperfusion injury associated with deep hypothermic circulatory arrest (DHCA), as well as the inflammatory response triggered by cardiopulmonary bypass (CPB). However, the relevance of both of these mechanisms is incompletely understood. To further characterize the cerebral ischemia-reperfusion and inflammatory reaction induced by CPB and DHCA, this study evaluated the cerebral expression of Lipocalin-2 (LCN2), an acute-phase protein expressed in various organs in response to ischemia-reperfusion along with other inflammatory mediators in a rat model of DHCA.

**Methods:** Male Sprague-Dawley rats were randomly assigned to three groups: DHCA group (n=10), sham group (n=8) and control group (n=3). DHCA animals were cooled to 18°C with CPB and underwent 60 min of DHCA, while sham animals were anesthetized, cannulated and heparinized without undergoing CPB/DHCA. Control animals were only anesthetized and their brains harvested. Brain samples from animals in DHCA and sham groups were obtained at 24 hours after CPB/DHCA or sham operation. The expression of LCN2 mRNA in the brain was analyzed by RT-PCR. Cerebral levels of LCN2 protein were determined by Western blot while in situ expression of LCN2 protein in the brain was analyzed by confocal microscopy. The levels of nuclear factor kappa-B (NF- $\kappa$ B) activation and of interleukin-1 $\beta$ ; (IL-1 $\beta$ ;) and interleukin-6 (IL-6) in the brain were measured by ELISA. Cerebral caspase-3 activation was analyzed by Western blot.

**Results:** Cerebral LCN2 mRNA was detected both experimental groups at 24 hrs after CPB/DHCA or sham operation with DHCA animals showing higher expression levels LCN2 compared to sham animals ( $p < 0.05$ ). The protein expression of LCN2 in the brain was similarly higher in DHCA animals compared to sham though not detected in control animals (Figure 1,  $p < 0.05$ ). Confocal microscopy identified LCN2 protein in astrocytes, choroidal epithelia and in endothelial cells of parenchymal vasculature but not in neurons. Cerebral levels of IL-1 $\beta$ , IL-6 and cleaved caspase-3 were higher in the DHCA group compared to sham ( $p = 0.06$ ;  $p = 0.04$ ;  $p < 0.05$ , respectively) but activity of NF- $\kappa$ B was similar between experimental groups.

**Conclusions:** These findings constitute the first report of upregulation of both, LCN2 mRNA and protein expression in response to ischemia-reperfusion 24 hours after CPB/DHCA. The abundance of the acute-phase protein LCN2 in astroglia and choroidal plexus suggests a role for LCN2 as part of the innate immune response to ischemia-reperfusion and cerebral inflammation. Lipocalin-2 may represent a novel therapeutic target in ameliorating perioperative cerebral injury following DHCA.

## CHANGES IN MYOCARDIAL CALCIUM CYCLING FOLLOWING LUNG RESECTION IN ELDERLY SWINE: THE POTENTIAL ROLE OF PHOSPHOLAMBAN DEPHOSPHORYLATION

Heerdt P; Wagner C; Park B; Hemmings H

*Memorial Sloan-Kettering Cancer Center; Weill Cornell Medical College*

The median age of patients presenting for resection of pulmonary malignancy in the United States is currently in excess of 70 years (1). Both clinical and experimental data indicate a decline in myocardial functional reserve with advancing age, in part due to decreased activity of the sarcoplasmic endoreticular calcium ATPase type 2a (SERCA2a), a key regulator of myocyte calcium cycling (2). Recent studies in young adult swine suggest that the age-related impairment of SERCA2a activity may be exacerbated following pulmonary lobectomy due to generation within the myocardium of peroxynitrite (ONOO), an inhibitor of SERCA2a (3). While it appears that the effect of ONOO on SERCA2a is at least partially the result of tyrosine nitration within the protein, ONOO may also impact SERCA2a activity by activating protein phosphatases (PP) which, in turn, dephosphorylate the SERCA2a regulatory protein phospholamban (PLB) (4). When dephosphorylated, PLB inhibits SERCA2a. The present study was designed to test the hypothesis that pulmonary resection during single lung ventilation in elderly swine is associated with decreased SERCA2a activity that occurs in conjunction with increased myocardial ONOO, PP activation and PLB dephosphorylation.

**Methods:** Myocardium harvested from 11 elderly Sinclair swine (>10 years of age with an expected life span of 12 years) were used for the study. Five animals had undergone left upper lobectomy during single lung ventilation with tissue obtained on the third postoperative day. The remaining 6 were non-operated controls. Tissue homogenates and/or SR isolates were prepared for HPLC analysis of 3-nitrotyrosine (3-NT), a stable product of ONOO, and Western blotting for SERCA2a, total PLB, and PLB phosphorylated at serine 16 (p-PLB). Values for p-PLB were normalized to total PLB, and are presented relative to SERCA2a expression. In addition, SR PP activity was determined using [32P] phosphorylase a as a substrate. Data were compared by t-test with  $p < 0.05$  considered significant, and presented as mean  $\pm$  SE.

**Results.** Pulmonary lobectomy was associated with a modest decline in SERCA2a activity (fig. panel A) and a marked rise in myocardial 3-NT (fig. panel B). As shown in figure panels C and D respectively, although there was a trend for PP activity to be higher, and p-PLB/SERCA2a to be lower, in the lobectomy animals, these trends were not statistically significant.

**Conclusions:** While the data indicate increased myocardial ONOO and decreased SERCA2a activity in elderly swine following lobectomy, they do not support the hypothesis of attendant changes in PP activity and decreased p-PLB/SERCA2a. Accordingly, results of the study are consistent with the concept that ONOO predominantly alters SERCA2a activity following lobectomy by direct nitration of the protein.

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## CLINICAL EVALUATION OF CENTRAL VENOUS CATHETER WITH INTEGRATED OXIMETRY FOR PATIENTS UNDERGOING ABDOMINAL AORTIC ANEURYSM SURGERY

Sawai T; Oka M; Nakahira J; Minami T

*Osaka Medical College*

**Background:** Central venous oxygen saturation (ScvO<sub>2</sub>) in the superior vena cava accurately reflects cardiocirculatory function, but is not always feasible in acute hemodynamic changes. We tested the accuracy of ScvO<sub>2</sub> values obtained by continuous ScvO<sub>2</sub> monitoring using an oximetry catheter, when compared with the ScvO<sub>2</sub> values obtained in vivo in the superior vena cava, during abdominal aortic aneurysm surgery.

**Patients and Methods:** After institutional approval and written informed consent was obtained, 10 adult patients undergoing abdominal aortic aneurysm surgery were enrolled in the study. After induction of general anesthesia, a central venous oximetry catheter (PreSep™ oximetry catheter, Edwards Lifesciences Ltd.) was inserted via the right internal jugular vein. The ScvO<sub>2</sub> was determined by both the continuous ScvO<sub>2</sub> monitoring method (ScvO<sub>2</sub>\_cath) and in vivo in the superior vena cava withdrawn from the distal lumen of the catheter (ScvO<sub>2</sub>\_blood), and measured at 4 points; after in vivo calibration, immediately after abdominal aortic cross clamp, declamping of the right iliac artery and declamping of the left iliac artery. At these same 4 points, cardiac output was measured by arterial pressure waveform analysis monitor (FloTrac/ Vigileo™). Linear regression analysis was performed by calculation of the correlation coefficient (r) between ScvO<sub>2</sub>\_cath and ScvO<sub>2</sub>\_blood. After normality was confirmed by normal distribution plots and histogram for the variables, the differences between the means of ScvO<sub>2</sub>\_cath and ScvO<sub>2</sub>\_blood was assessed by Bland-Altman analysis. Bias was represented by the mean of differences between ScvO<sub>2</sub>\_cath and ScvO<sub>2</sub>\_blood. Precision was represented by standard deviation (SD) of the differences. A percentage error between the measurements of ScvO<sub>2</sub>\_cath and ScvO<sub>2</sub>\_blood was calculated.

### Results

A total 40 points of ScvO<sub>2</sub>\_cath and ScvO<sub>2</sub>-blood were analyzed. At each point, bias and precision between ScvO<sub>2</sub>\_cath and ScvO<sub>2</sub> were 2.84% and 6.88% (r=0.89), 1.63% and 5.9% (r=0.91), -0.02% and 3.37% (r=0.99), 0.11% and 3.85% (r=0.98), respectively. At each point, the percentage error between ScvO<sub>2</sub>\_cath and ScvO<sub>2</sub>\_blood was 18.2%, 14.4%, 8.6% and 9.5%, respectively. (Table).

### Conclusions

Central venous oximetry catheter provides accurate continuous ScvO<sub>2</sub> monitoring in patients undergoing abdominal aortic aneurysm surgery corresponding against acute hemodynamic changes.

## CLINICAL RISK FACTORS FOR PERSISTENT PAIN AFTER THORACOTOMY: A MULTIVARIATE LOGISTIC REGRESSION RISK PREDICTION MODEL.

Aeschlimann N; Tong B; White W; Hill S; Grichnik K; Shaw A

*Duke University*

### Introduction

Acute pain is a normal response to traumatic injury and protects the individual from exposure to further harm. In contrast, chronic pain is a maladaptive response caused by aberrations in the normal repair and regeneration mechanisms that lead to healing after injury. Post thoracotomy pain syndrome (PTPS) is a particularly troublesome clinical problem, affecting somewhere between 30-70% of patients. This syndrome likely has clinical, behavioral and genetic determinants. In order to identify the relevant clinical factors (to pave the way for future genetic studies) we have developed a clinical risk prediction model for PTPS.

### Methods

With approval from the Duke IRB, quality-of-life questionnaires were given at clinic visits before lung resection surgery and also at 3, 6 and 12 months after surgery. Patients were asked "In the past month, on average, how intense was your pain on a score from 0-10?" Significant post-operative pain was defined as a visual analog scale (VAS) response of 3 or higher on this question at any time after surgery. Preoperative patient and clinical characteristics (identified from a clinical database) were then tested for association with the occurrence of post-operative pain with independent chi-squared tests, and jointly in a multivariate logistic regression analysis. Two-way interactions between terms were also tested.

### Results

Postoperative pain and clinical data were available for 864 patients. Of these, 362 (42%) had significant postoperative pain defined as above. The characteristics tested are shown in table 1, with the p-value from the univariate chisquared test of association. The multivariable logistic regression model tested all of these potential predictors together, dropping non-significant terms one at a time starting with the least significant. Two-way interactions between terms were also tested before a non-significant term was dropped.

The Spearman (rank) correlation of age with greatest postoperative average pain was significant ( $p < 0.0001$ ) and negative (pain decreased as age increased). The incidence of post-operative pain was lower in higher decades of age (table 1). The effect of preoperative pain was most pronounced in lobectomy cases (interaction  $p = 0.0140$ ). More patients who had received chemotherapy developed pain when the surgery was a wedge resection (interaction  $p = 0.0048$ ). In patients without chemotherapy, fewer Caucasians had pain than other ethnicities (interaction  $p = 0.0427$ ). The area under the ROC curve for the model including these interactions was 0.739 (figure 1), indicating reasonable discrimination of PTPS cases.

### Conclusions

The clinical characteristics that appear to independently predict PTPS are preoperative pain score, age, disease stage, use of adjuvant chemotherapy and race. The predictive value of this model is 0.739. We are currently validating this model in a population of patients from a different institution, and in future studies we will incorporate genetic and behavioral variables in an effort to improve prediction and permit better patient stratification in subsequent clinical intervention trials.

## COMPARATIVE STUDY OF HEMOSTATIC PRODUCTS IN THE REVERSAL OF WARFARIN ON THROMBOELASTOMETRY (ROTEM™)

Rumph B; Bolliger D; Szlam F; Levy J; Tanaka K

*Emory University*

**Introduction:** Warfarin therapy is used in prevention of thrombotic complications associated with atrial fibrillation, mechanical heart valves, and deep venous thrombosis. For urgent and emergent surgical procedures, warfarin therapy may increase the risk of hemorrhagic complications. Current guidelines in the United States recommend administration of vitamin K and fresh frozen plasma (FFP) for acute reversal because prothrombin complex is not available for this indication. [SPCHAR(sup1)] We compared in vitro procoagulant effects of FFP, cryoprecipitate, and platelet concentrate in warfarin-treated plasma using thromboelastometric technique.

**METHODS:** After IRB approval, FFP, cryoprecipitate, and platelets were obtained from the local blood bank, and mixed with warfarin-treated plasma with INR between 2.8 and 3.8 (King George Biomedical, Overland Park, KS). All three blood products were mixed at 25, 50, and 100 µl with warfarin plasma at 275, 250, and 200 µl, respectively, to simulate transfusion of 8.3%, 16.7%, and 33.3% of plasma volume. Hemostatic effects were evaluated with thromboelastometry (ROTEM™, Pentapharm, Munich, Germany). Coagulation was triggered with 20 µl of 20 mmol CaCl<sub>2</sub> and 2 µl of tissue factor (TF, 0.1%). Onset of clotting (clotting time; CT sec), rate of fibrin polymerization (angle; &#945;°), and maximal clot firmness (MCF; mm) were measured.

**RESULTS:** At the highest dose, all three products significantly improved CT (Figure 1). Cryoprecipitate at the highest dose shortened CT significantly more than FFP (134[SPCHAR(plusmn)]19.3 vs. 217[SPCHAR(plusmn)]49.6 sec). Cryoprecipitate and platelets also dose-dependently increased the angle from 22.4° to 61.4°[SPCHAR(plusmn)]3.5 and 22.4° to 43.3°[SPCHAR(plusmn)]11.0, respectively (p<.05). Cryoprecipitate and platelets also dose-dependently increased MCF from 20.0 mm to 52.6[SPCHAR(plusmn)]6.5 mm and from 20.0 mm to 64.9[SPCHAR(plusmn)]5.9 mm, respectively (p<.05; Figure 2). In contrast, the addition of FFP did not increase angle or MCF in any dosage.

**DISCUSSION:** Our in vitro study of hemostatic transfusion products demonstrated that cryoprecipitate and platelets improve clot formation on ROTEM™ in a dose-dependent manner. The addition of FFP did not significantly improve any parameter, except shortening CT at the highest transfusion volume (equivalent to 1L transfused). Because perioperative coagulopathy is often accompanied by a dilutional decrease in platelets and coagulation factors, (particularly fibrinogen)[SPCHAR(sup2)], FFP may not be effective in reversing perioperative coagulopathy in warfarin-treated patients. It is prudent to reevaluate the efficacy of FFP for warfarin-reversal.

**REFERENCES:** [SPCHAR(sup1)]Ansell, et al. Chest:2008; [SPCHAR(sup2)]Hiippala, et al. Anesth Analg:1995

## COMPARISON OF METHODS TO CLEAR LIPID DEBRIS FROM PACKED RED BLOOD CELL UNITS

Lemons J; Welsby I; Ing R; Jordan L; Smigla G

*Duke University Medical Center*

### Introduction:

Packed red blood cells (pRBCs) undergo many changes with storage that can have undesired consequences. As red blood cells age, they gradually express phosphatidylserine (PS) on their surface, which is usually confined to the inner membrane. The expression of such phospholipids will lead to accumulation of lipid debris with increased procoagulant activity within the stored red blood cell unit. The clearance of such debris prior to transfusion could be beneficial for patients. We propose that such procoagulant lipid debris can be cleared from pRBCs by the use of commonly used cellsaver washing devices.

### Methods:

Four expired units of pRBCs were obtained from the American Red Cross and pooled. Using flow cytometry, Annexin V antibody binding was assessed for unwashed pRBCs as well as pRBCs washed using three devices (Cobe BRAT II, Fresenius CATS II, and Cobe 2991 Blood Cell Processor). The blood bank washing device (Cobe 2991) was used as the gold standard and the unwashed pRBCs were used as a negative control.

### Results:

The standard blood bank washing device showed the greatest effect of removing lipid debris present in the unwashed pRBCs demonstrated by a reduction in the % gated from 24.2% in the unwashed pRBC pool to 3.6% in the blood bank washed sample. Figures 1A and 1B represent the flow cytometry results for unwashed and blood bank washed pRBCs, respectively. The graphs are gated by front and side scatter marking debris size (red = RBC, blue = cellular debris). The graphs demonstrate a reduction in the amount of debris present in the blood bank washed pRBCs as compared to the unwashed pRBCs. The Fresenius CATS II cellsaver showed a reduction to 8.7%, followed by the Cobe BRAT II which showed a reduction to 18.5%.

### Conclusion:

Flow cytometry using Annexin V binding demonstrated that expired pRBCs contain lipid debris that binds Annexin V. We were able to demonstrate that this debris could be removed by the use of commercially available cellsaver and cellwashing devices. The standard blood bank washing device showed the greatest effect of removing such debris, followed by the Fresenius CATS II cellsaver and Cobe BRAT II, respectively. Further experiments need to be conducted to determine at which point in the life of a pRBC unit such debris begins to appear. Also, it must be shown that the presence of such lipid debris is harmful and thus by removing this debris a potential benefit could be offered to patients receiving blood transfusions.

## COMPARISON OF THE PHARMACOKINETICS AND PHARMACODYNAMICS OF CLEVIDIPINE AND NICARDIPINE

Aronson S; Mould D; Dasta J; Franklin H

*Duke University Medical Center; Projections Research Inc; The Medicines Company; University of Texas*

**BACKGROUND:** Tight blood pressure (BP) control during cardiac surgery has been shown to reduce adverse outcomes occurring within 30 days of surgery.[1] Clevidipine butyrate IV emulsion (CLV) and nicardipine (NIC) are 2 dihydropyridine antihypertensive agents used to control perioperative BP. They are metabolized and eliminated via different processes; CLV is rapidly metabolized by esterases in the blood and extravascular tissue, while NIC is metabolized via the cytochrome P450 pathway. Thus, CLV has an ultrashort initial half-life of approximately 1–2 min and terminal half-life of 22 min, and follows direct effect pharmacodynamics (PD) allowing for rapid onset (2–3 min) and offset of effect. Once CLV is discontinued, return to baseline BP is rapid and independent of dosage and duration of infusion.[2] In contrast, NIC has a longer initial half-life of 45 min and terminal half-life of between 11.5 and 16 h. This investigation compares the pharmacokinetic (PK) and PD properties of CLV and NIC.

**METHODS:** Nonstochastic simulations of PK and PD versus time for CLV and NIC were conducted using the program Stella, v8.1.1. The PK model for CLV (2-compartment linear) was based on a prior model for this agent in hypertensive patients. The PD model for CLV combined the PK model with a linear direct-effect PD model and was used for 2 different base cases. The up-titration scheme for CLV infusion ranged from 2.0–32.0 mg/h, achieved by doubling the infusion rate every 1.5 min (Case A) or every 3 min (Case B). For NIC, published mean PK data [3] were digitized and fitted into a 2-compartment model; a linear model was used to describe PD. The NIC simulation was performed using the recommended dosage for rapid BP reduction with adjustments every 5 min. CLV and NIC were up-titrated until the target systolic BP (SBP) between 140 and 160 mmHg was reached, and the infusion was maintained thereafter for a total of 12 h. SBP was evaluated over 24 h for CLV and 36 h for NIC. Three scenarios with baseline SBP (180, 220, 260 mmHg) were evaluated.

**RESULTS:** CLV administration was associated with rapid SBP control (table), regardless of baseline SBP. Following cessation of CLV, SBP returned to baseline values within 9 h. Time to reach target SBP with NIC was 30 and 72 min for those with a baseline SBP of 180 or 220 mmHg, respectively; for those with a baseline SBP of 260 mmHg, however, the target was never achieved. Following cessation of NIC, SBP failed to return to baseline levels over the 24-h period.

**CONCLUSION:** Owing to its ultrashort half-life and rapid onset and offset of action, CLV may provide more precise control of BP compared with NIC and more rapid offset of effect using simulation data from the clinical setting. This may permit a rapid transition to oral antihypertensives using CLV.

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## CONTINUOUS MONITORING OF CEREBRAL BLOOD FLOW AUTOREGULATION DURING CARDIAC SURGERY IN ADULTS WITH NEAR INFRA-RED SPECTROSCOPY: PRELIMINARY RESULTS

Hogue C; Johsi B; Brady K; Stearns J

*The Johns Hopkins Hospital*

**Introduction:** Cerebral hypoperfusion during cardiac surgery is of growing importance as a cause of brain injury due to the increasing proportion of elderly patients with cerebral vascular disease.(1, 2) Individualizing mean arterial pressure (MAP) to be within the patient's autoregulatory range during cardiopulmonary bypass (CPB) would more likely ensure adequate cerebral blood flow (CBF) than the standard practice of empirically targeting MAP to > 50 mmHg. In this study we evaluate whether real-time monitoring of CBF autoregulation using near infra-red spectroscopy (NIRS) accurately detects the lower autoregulatory threshold compared with a validated, but technically more challenging method using transcranial Doppler (TCD). (1)

**Methods:** Fifty-four patients > 50 years undergoing CABG and/or valve surgery with CPB were enrolled in an IRB approved protocol after giving written informed consent. Bilateral middle cerebral artery TCD monitoring and NIRS monitoring were performed with the INVOS device (Somenetics Corp, Troy, MI) or Fore-Sight device (CAS Medical Systems, Branford, CT) in 37 and 17 patients, respectively. Arterial pressure, TCD, and NIRS signals were sampled with an analog-to-digital converter at 58 Hz and down loaded to a personal computer.(2) The TCD and NIRS signals were time integrated as non-overlapping 10-sec mean values to eliminate noise from the respiratory and pulse frequencies. A continuous, moving Pearson correlation coefficient was calculated between MAP and TCD CBF velocity and NIRS signals rendering the variables mean velocity index (Mx) and cerebral oximetry index (COx), respectively. Consecutive, paired, 10-sec averaged values from 300-sec duration were used for each calculation, incorporating 30 data points for each index. When CBF is autoregulated, there is no correlation between CBF and MAP (i.e.,  $Mx < 0.2$  and  $COx < 0.3$ ), but when pressure passive, Mx and COx are positively correlated with MAP.(3) The lower CBF autoregulation threshold was defined as the MAP where Mx was  $>0.2$  and COx was  $> 0.3$ .(4) The MAP at the lower autoregulatory threshold detected by Mx or COx were compared using ANOVA.

**Results:** The MAP at the autoregulatory threshold (range 40 to 80 mmHg) detected with Mx and COx (Figure) was not different:  $66 \pm 14$  mmHg and  $67 \pm 12$  mmHg, respectively. In 99% of patients, the lower autoregulatory threshold detected by COx was within 5 mmHg of that detected by Mx.

**Conclusion:** These data suggests that NIRS based COx monitoring provides an accurate detection of the lower CBF autoregulatory threshold in patients undergoing cardiac surgery. This promising non-invasive monitoring method might provide a means for individualizing MAP during surgery potentially reducing the frequency of brain injury due to cerebral hypoperfusion.

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## CORRELATION BETWEEN MIXED VENOUS OXYGEN SATURATION AND ANESTHETIC DEPTH DURING CARDIOPULMONARY BYPASS

Stein E; Minhaj M; Glick D; Karl L; Tung A

*University of Chicago*

**Introduction:** During cardiopulmonary bypass, mixed venous oxygen saturations (SvO<sub>2</sub>) often fluctuate in the absence of changes in temperature or cardiac output. One explanation for these changes has been changes in anesthetic depth and consequently brain metabolism. Existing evidence suggests that increased anesthetic depth decreases cerebral metabolic rate and brain oxygen consumption. Reductions in cerebral metabolic rate resulting from increased anesthetic depth would thus result in decreased whole body oxygen consumption and an increased SvO<sub>2</sub>. Although a relationship has been suspected, no data currently exist examining the relationship between mixed venous oxygen saturation (SvO<sub>2</sub>) and depth of anesthesia. We hypothesized that changes in anesthetic depth would correlate with changes in whole body oxygen consumption. To test this hypothesis, we correlated measurements of mixed venous oxygen saturation with anesthetic depth (as measured by the BIS monitor) in patients undergoing cardiopulmonary bypass.

**Methods:** This study was performed as part of a larger study involving the BIS monitor (Aspect Medical Systems) and anesthetic depth. Patients having surgery involving cardiopulmonary bypass were consented, in accordance with IRB protocol. The BIS monitor was placed prior to the start of cardiopulmonary bypass and bispectral index values were measured continuously during the bypass period. Measured variables included the BIS value, SvO<sub>2</sub>, patient body temperature, mean arterial pressure, blood inhaled anesthetic levels, cardiac output, hematocrit, and arterial PO<sub>2</sub>. Along with the above variables, the SvO<sub>2</sub> was measured at five minute intervals during cardiopulmonary bypass using a real-time blood gas monitor (CDI monitor, Terumo Systems Cardiovascular, Corp.). The Pearson correlation (R<sup>2</sup>) coefficient was calculated to determine the relationship between the SvO<sub>2</sub> and bispectral index at intervals when stability among hematocrit ( $\pm 2\%$ ), temperature ( $\pm 10^\circ\text{C}$ ), constant blood inhaled anesthetic level, constant FiO<sub>2</sub>, and constant cardiopulmonary bypass pump flow rates existed for each subject.

**Results:** Twenty-three patients were studied; 6 underwent CABG, 9 underwent valve or aortic repair procedures, 5 underwent combined valve repair and CABG, 2 underwent left ventricular assist device placement, and 1 had an IVC thrombectomy. The average age was 65 years and average temperature during bypass was 34.6C. Between 10 and 30 simultaneous measurements of SvO<sub>2</sub> and bispectral index were obtained per patient. The Pearson coefficient was calculated for each patient. The average Pearson coefficient was  $0.002 \pm 0.320$  ( $p > 0.05$ ).

**Discussion:** In twenty-three patients undergoing cardiac surgery, we did not find a statistically significant relationship between bispectral index values and SvO<sub>2</sub>. Our data were obtained while hematocrit, temperature, blood inhaled anesthetic level, FiO<sub>2</sub>, and cardiopulmonary bypass pump flow rates were stable for each subject. These data suggest that during cardiopulmonary bypass, other factors besides depth of anesthesia may cause mixed venous oxygen levels to change.

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## CU-2010 - A NOVEL ANTIFIBRINOLYTIC PROTEASE INHIBITOR DISPLAYS ALSO ANTICOAGULANT PROPERTIES

Dietrich W; Nicklisch S; Koster A; Spannagl M; van de Locht A

*German Heart Center Berlin; The Medicines Comp.; Working Group on perioperative Hemostasis*

**Background:** Antifibrinolytics are widely used in cardiac surgery to reduce bleeding and transfusion requirement. However, one antifibrinolytic, the protease inhibitor aprotinin, was suspected to cause severe side-effects and was removed from marketing (1). CU-2010 is a novel, small synthetic compound (MW 700 Da) with peptide-like characteristics that allow substrate-like binding to the active site of serine proteases. It has proven antifibrinolytic properties (2). Beyond its primary targets, plasmin and plasma kallikrein, CU-2010 as a serine protease inhibitor also inhibits enzymes of the coagulation cascade (2). The attenuation of enzyme activity upstream in the coagulation pathways might mitigate inadvertent coagulation activation during cardiac surgery. CU-2010 is in development for the use as antifibrinolytic in cardiac surgery. This in vitro study investigates possible anticoagulant potency of this compound.

**Methods:** With informed consent, the blood from 8 healthy donors was mixed with different concentrations of CU-2010 and unfractionated heparin was added in ascending concentrations. Heparin response was determined and TEG analysis was performed. Additionally, heparin-containing blood from cardiac surgical patients was mixed with CU-2010 and ACT response was recorded.

**Results:** CU-2010 resulted in a dose-dependent increase in heparin response in all experiments. Heparin response as measured by Hepcon HMS kaolin-based ACT was increased in the presence of CU-2010 (Figure). TEG reaction time was prolonged after intrinsic and extrinsic activation. Heparin requirement was reduced by CU-2010.

**Discussion:** This study demonstrates a dose-dependent attenuation of the extrinsic pathway of coagulation as measured by the ACT and TEG. CU-2010 is a serine protease inhibitor, which, besides its antifibrinolytic potency, also attenuates activation of coagulation. CU-2010 also demonstrated these anticoagulant properties as was expected from its specificity for plasma kallikrein and particularly for factor Xa (2). The inhibition of procoagulant enzymes is of interest because the activation of thrombin plays a central role in CPB-related coagulopathy. It remains to be demonstrated whether this potential advantage translates into clinical benefit for the patient.

(1) N Engl J Med 2008; 358: 2319

(2) Anesthesiology 2009;110:1

## DECREASED CEREBRAL TISSUE OXYGEN SATURATION DURING AORTIC SURGERY INCREASES RISK OF POST-OPERATIVE COMPLICATIONS

Fischer G; DiLuozzo G; Lin H; Griep R; Reich D

*Mount Sinai School of Medicine*

**Introduction:** Currently only limited information exists exploring the relationship between brain oxygenation levels during aortic surgery and post-operative outcomes (1). The FORE-SIGHT® (CAS Medical Systems, Branford CT USA) cerebral oximeter measures absolute cerebral tissue oxygen saturation (SctO<sub>2</sub>) values. We hypothesized that a relationship exists between decreased intraoperative SctO<sub>2</sub> values and post-operative complications following aortic surgery.

**Methods:** With IRB approval and informed consent, patients undergoing elective thoracic aortic surgery with deep hypothermic circulatory arrest (DHCA) were monitored intraoperatively using the FORE-SIGHT. Two sensors were placed on the subject's forehead bilaterally with SctO<sub>2</sub> values recorded every 2 seconds starting after induction of anesthesia until the end of surgery. SctO<sub>2</sub> minutes and the area above the curve (AAC) spent beneath the absolute threshold limits of 50, 55, 58, 60, & 65% were computed for both left & right sensors. Complications were categorized as "major" (death, stroke, depressed LV function, respiratory failure, sepsis, delirium, renal failure, GI complications, or severe volume overload) and "minor" (atrial fibrillation, minor volume overload, phlebitis, or none). Post-operative complications, Extubation time, ICU length of stay, and Hospital length of stay (HLOS) data were collected and compared to SctO<sub>2</sub> data and DHCA time.

**Results:** Demographics: 30 subjects; Gender 22M/8F; Race 25W/1AA/3HS/1IN; Post-induction SctO<sub>2</sub> was 70.6% (SD 5.1). SctO<sub>2</sub><60% (minutes & AUC), SctO<sub>2</sub><58% (minutes), and DHCA minutes were significantly associated with Extubation time and ICU LOS ( $p<0.05$  two-tailed, Spearman). Major complications significantly correlated ( $p<0.05$  two-tailed, Spearman) to Extubation time (median: 3 days vs 1 day for subjects with major complication) and HLOS (median: 13 days vs 7.5 days). Logistic regression odds ratio analysis showed that for every increment of 30 minutes below a SctO<sub>2</sub> threshold, the risk for major complications increased 2.1 times for SctO<sub>2</sub><60% and 3.7 times for SctO<sub>2</sub><55% (Table 1). Similar results were found for AAC of SctO<sub>2</sub> thresholds with 50 minute-% increments. Also for every 5 minutes of DHCA, the risk of major complications increased 1.6 times.

**Discussion:** Despite the low number of subjects enrolled in this study, decreased SctO<sub>2</sub> values and prolonged DHCA times were found to be associated with major complications, prolonged extubation times, and ICU/Hospital LOS. This study suggests that prolonged intraoperative periods of time with SctO<sub>2</sub><60% correlate significantly with an increased risk of having major complications and an increased LOS.

This study was partially supported by NIH grant NS045488.

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## DECREASED FOREBRAIN CEREBRAL TISSUE OXYGEN SATURATION IS ASSOCIATED WITH COGNITIVE DECLINE AFTER CARDIAC SURGERY

MacLeod D; White W; Newman M; Ikeda K; Mathew J

*Duke University Medical Center*

**Introduction:** In this exploratory, non-interventional observational study, we examined the relationship of cerebral tissue oxygen saturation (SctO<sub>2</sub>) measured by the FORE-SIGHT® cerebral oximeter (CAS Medical Systems, Branford CT USA) to postoperative cognitive decline (POCD).

**Methods:** With IRB approval and informed consent, 60 subjects undergoing coronary bypass surgery (CABG) and/or valvular surgery (VS) were enrolled in the study. Exclusions were history of symptomatic cerebrovascular disease, uncontrolled hypertension, alcoholism, psychiatric illness, creatinine >2 mg/dL, <7th grade education, were pregnant, or baseline MMSE score <24. Bilateral sensors were placed on the subject's forehead from pre-induction to chest closure, with SctO<sub>2</sub> recorded every two seconds. SctO<sub>2</sub> minutes and area under the curve (AUC) below absolute thresholds 50, 55, 58, 60, & 65% were computed for L & R sensors. Subjects were examined with a battery of five cognitive tests a day before surgery and 6 weeks post surgery. The test battery consisted of the Short story module of the Randt Memory Test, Modified Visual Reproduction Test (WAIS-R), Digit Span subtest (WAIS-R), Digit Symbol subtest (WAIS-R), and Trail Making Test (Part B) which produced 10 scores. A factor analysis of the 10 test scores returned four independent cognitive domain scores: 1) verbal memory & language comprehension, 2) figural memory, 3) attention & concentration and 4) psychomotor & processing speed. These were averaged for an overall cognitive index, and domains 2, 3, and 4 were averaged as a separate summary score. The association between the various SctO<sub>2</sub> measures and the 6-week change in cognitive scores was tested by Spearman rank correlation and by multivariable linear regression accounting for baseline cognitive score, age, gender, and years of education. Diabetes, crossclamp time, CPB time and CPB temperature were also tested as single covariates with SctO<sub>2</sub> in separate regression models.

**Results:** 53 subjects completed all testing. Of these, 18% underwent CABG+VS, 32% were female, 87% were Caucasian, and 32% were diabetic. The pre-induction SctO<sub>2</sub> was lower in patients undergoing valvular surgery (67.0% vs 72.1%; p=0.01). Declines in SctO<sub>2</sub> below several thresholds were significantly associated with 6-week decline in the Domain 2, 3, & 4 average in unadjusted Spearman correlations (Table 1). After adjustment for baseline variables SctO<sub>2</sub> minutes <60% remained significantly associated with this cognitive decline (p=.040, R-Squared=.09). Verbal memory (Domain 1), measured by the Randt test, was not associated with decreased SctO<sub>2</sub>.

**Conclusion:** Decreases in intraoperative SctO<sub>2</sub> are associated with POCD. The lack of association with Domain 1 is explained by the fact that the Randt test is typically associated with temporal and parietal lobe function and thus not measured by a monitor of frontal lobe cerebral tissue oxygen saturation.

## DECREASED POSTOPERATIVE FLOW PROPAGATION VELOCITY IS ASSOCIATED WITH A NEED FOR INOTROPIC SUPPORT AFTER CORONARY ARTERY BYPASS SURGERY

Poppers J; Shook D; Weinmann M; Perry T; Sherman S; Body S

*Brigham and Women's Hospital*

### Background

Transient diastolic dysfunction is common after coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB). We hypothesized that decreased flow propagation velocity (Vp) in patients with preserved systolic function after CABG surgery is associated with increased inotropic requirement in the immediate postoperative period.

### Methods

After institutional review board approval, we conducted a prospective observational study to examine the association between Vp, a relatively load-independent measure of diastolic function, and the need for postoperative inotropic support in 12 patients undergoing primary CABG surgery with CPB. Using transesophageal echocardiography (TEE), we recorded Vp, and fractional shortening (FS) (as a measure of systolic function) prior to sternotomy and after sternal closure. Our primary outcome was defined as any pharmacologic inotropic support on arrival to the intensive care unit (ICU). We defined diastolic dysfunction as Vp <45cm/s and systolic dysfunction as FS <25%.

### Results

Three patients developed postoperative systolic dysfunction, and were therefore excluded from further analysis. Six of the remaining nine patients (67%) had Vp <45cm/s following sternal closure, consistent with diastolic dysfunction. The incidence of inotropic use on arrival to the ICU was 33%. Vp was lower in patients who required postoperative inotropic support compared with patients who did not (Median [IQR]; 26.7 cm/s [25.0-30.4] vs. 40.1 cm/s [34.5-56.2], P=0.053) (see Figure).

### Conclusion

In this small pilot study, we demonstrate that in patients with preserved postoperative systolic function after undergoing primary CABG with CPB, decreased Vp after chest closure is associated with inotropic use upon arrival to the ICU.

## DEEPER LEVEL OF ANESTHESIA IS ASSOCIATED WITH ADVERSE NEUROLOGICAL OUTCOMES IN CARDIAC SURGICAL PATIENTS

Karri S; Duncan A; Koch C; Maheshwari A; Xu M

*Cleveland Clinic*

**Introduction:** Recent reports have suggested that depth of anesthesia as measured by bispectral index (BIS) may affect postoperative outcomes. For example, increased depth of anesthesia was associated with increased one year mortality following noncardiac surgery.(1) Others have reported improved postoperative recovery of cognitive function with deeper levels of anesthesia.(2) The influence of anesthetic depth on outcomes following cardiac surgery has not been examined. The purpose of this investigation was to assess the influence of anesthetic depth as measured by BIS on postoperative neurological outcomes in cardiac surgical patients.

**Methods:** 4577 patients underwent cardiac surgery from March 29, 2006 to May 31, 2007. Intraoperative BIS levels, collected from time of incision until end of surgery, were examined to determine whether depth of anesthesia was associated with postoperative neurological complications. The mean and median BIS values and the percentage of time that the patient's BIS score was  $\geq 4$ ;  $\geq 5$  (%BIS $\geq 4$ ;  $\geq 5$ ) were calculated and the relationship to neurologic morbidity (defined as a new postoperative focal or global deficit  $\geq 5$ ; 24 hrs) was examined. Forty-two baseline and perioperative variables were included in a univariable analysis, and variables with univariate P-value of  $>0.10$  were not used in the multivariable analysis. The remaining variables were set into the logistic regression model and backward selection procedure was used to assess the association between BIS and neurologic morbidity by forcing the variable of interest (median BIS, mean BIS, %BIS $\geq 4$ ;  $\geq 5$ ) into the model.

**Results:** BIS was recorded approximately every  $14.4 \pm 2.3$  min. Neurologic morbidity was observed in 67 (1.5%) patients. Patients with neurologic morbidity had a lower median BIS (25th, 75th%) compared with patients without neurologic morbidity [41(39,43.5) vs. 43 (40,47), $P = 0.003$ ]. Patients with neurologic morbidity had a greater percent of time at deeper levels of anesthesia. (%BIS $\geq 4$ ;  $\geq 5$  was 0.8(0.6,0.9) in patients with neurologic morbidity vs. 0.7(0.4,0.9) in patients without neurologic morbidity;  $P = 0.005$ ]. The risk-adjusted odds ratio (95%CI) of neurological morbidity for mean and median BIS (per 10 units increase) was 0.504(0.333, 0.763;  $P=0.0012$ ) and 0.564 (0.370,0.859;  $P = 0.0077$ ), respectively. The odds ratio (95% CI) of %BIS  $\geq 4$ ;  $\geq 5$  was 3.678(1.359, 9.955;  $P = 0.0104$ ).

**Conclusion:** Deeper levels of anesthesia as measured by BIS were associated with worse postoperative neurological outcomes in cardiac surgical patients.

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## DO INSULIN-SENSITIZING ORAL HYPOGLYCEMICS INFLUENCE POSTOPERATIVE OUTCOMES IN TYPE 2 DIABETIC PATIENTS UNDERGOING CARDIAC SURGERY?

BUSTAMANTE S; DUNCAN A; XU M; O'CONNOR M

### CLEVELAND CLINIC

**BACKGROUND:** Diabetes mellitus increases risk for adverse outcomes following cardiac surgery. Treatment of type 2 diabetes often includes oral hypoglycemics, which have additional non-hypoglycemic systemic effects. Sulfonylureas are insulin secretagogues that block cardiac ATP-dependent K<sup>+</sup> channels preventing ischemic preconditioning and myocardial protection. Alternatively, insulin sensitizing agents (thiazolidinediones, biguanides) have been ascribed to have cardiovascular benefits including decreased blood pressure, improvement of dyslipidemia, enhanced fibrinolysis, decreased vascular inflammation and smooth muscle cell proliferation. Previously, we reported that diabetic patients treated with metformin, an insulin sensitizing agent, was associated with improved postoperative outcomes (1). The purpose of this analysis was to evaluate whether diabetic patients treated with insulin sensitizing agents as compared with insulin secretagogues had improved outcomes after cardiac surgery.

**METHODS:** The study population included 580 type 2 diabetics, who underwent cardiac surgery between October 2005 and May 2007 and were categorized into two groups: treatment with insulin sensitizing agents (thiazolidinediones, biguanides) +/- other antidiabetic agent (insulin-sensitizer group; ISN) vs sulfonylureas (insulin secretagogue group; ISG). Postoperative outcome variables included in-hospital mortality and the following morbidities: 1)cardiac: myocardial infarction/low cardiac output requiring mechanical circulatory support; 2)neurologic: focal or global neurologic deficit; 3)prolonged intubation:(>72hr); 4)renal: anuria or institution of renal dialysis; 5)infection: pneumonia, mediastinitis, wound infection, or septicemia; 6)overall morbidity: incidence of one or more of the above morbidities including death. A propensity score was calculated for each patient from a logistic model including 42 baseline and perioperative variables. The C-statistics for propensity model was 0.733. The two groups were matched using the Greedy matching technique. Outcomes were compared with Chi-square test, Fisher's exact and Wilcoxon's ranked sum test.

**RESULTS:** There were 382 patients taking ISN and 198 taking ISG agents. Univariate analysis for unmatched patients demonstrated that ISN had less prolonged intubation [30/382(7.9%) vs 30/198(15.2%); p= 0.006], serious infection [10/382(2.6%) vs 16/198(8.1%); p=0.003] and overall morbidity [42/382(11.0%) vs 36/198(18.2%); p=0.016]. Mortality and other morbidities were similar between groups. One-hundred-fifty ISN patients (39%) were 1:1 propensity matched to ISG patients. Average blood glucose levels were not different between groups. No difference was observed between matched patients in terms of mortality and cardiac, neurologic, prolonged intubation, renal, infection and overall morbidity.

**CONCLUSION:** Although previous evidence suggests that insulin sensitizing agents may have cardioprotective effects in contrast to potential detrimental effects of sulfonylureas, our investigation did not find a difference in clinical outcomes in diabetic patients treated with insulin sensitizing agents compared with insulin-secretagogues following cardiac surgery.

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## DO TEG HEPARINASE CUPS ADEQUATELY NEUTRALIZE CARDIOPULMONARY BYPASS LEVELS OF HEPARIN?

Rhee A; Shore-Lesserson L; Rhee A; Shore-Lesserson L; Bello R; Setty S; D'Alessandro D

*Montefiore Medical Center; Montefiore Medical Center*

Intro: The thromboelastogram (TEG) is a point of care test used to assess a patient's ability to form clot. When a patient is receiving heparin, TEG analysis requires heparin neutralization with heparinase. Originally, a heparinase bullet that contained 4 international units (IU) of heparinase was used and said to reverse 6 IU of heparin per ml of blood. Current technology is limited to a heparinase cup. This cup contains 2 IU of heparinase, but should also reverse up to 6 IU heparin per ml of blood. Inadequate reversal of heparin with heparinase could lead to falsely abnormal TEG results and the inappropriate treatment of patients with drugs and blood products.

Patients requiring cardiac surgery with cardiopulmonary bypass receive large doses of heparin that result in blood/plasma concentrations of approximately 2-5 IU heparin per ml. The heparinase cups are described to have the capacity to neutralize this amount of heparin. We sought to determine whether the new TEG cups contain enough heparinase to neutralize the heparin in the blood of cardiopulmonary bypass patients.

Method: In a single-center, prospective, non-randomized, study, patients undergoing cardiac surgery had 10ml of blood collected prior to incision. A portion of that blood sample was used to run a baseline TEG using a plain cup and kaolin (360 mcl sample volume). We then took another portion of that blood sample and added incrementally increasing amounts of heparin in vitro to produce blood heparin concentrations of 2-8 IU/ml. These dilutions were performed in a 1000 mcl bullet by exchanging 3 mcl of whole blood for 3 mcl of the total heparin concentration needed to achieve our desired final concentration. The sample volume in the TEG was kept at 360 mcl for each assay. TEGs were performed on these samples using kaolin and heparinase cups to neutralize the heparin that was added in vitro. We used a paired t-test to compare difference in TEG R times between the baseline and different heparin concentrations. Results: We found that there was no significant difference in the TEG R value between the baseline sample (no heparin) and the blood samples with 2U/ml of heparin added to them ( $6.39 \pm 1.34$  vs.  $7.29 \pm 1.66$ ,  $p = .053$ ). However, there was a statistically significant difference in the R value between the baseline TEGs and all of the TEGs which had 3 - 8 IU/ml of heparin added to them. For example at 5 IU/ml, the R value was  $8.26 \pm 2.70$  vs.  $6.60 \pm 1.41$  at baseline,  $p = 0.0002$ . At 8 IU/ml of heparin, the R value is  $8.67 \pm 2.42$  vs.  $6.75 \pm 1.40$ ,  $p < 0.00002$ .

Discussion: Our data show that heparinase cups do not sufficiently neutralize heparin concentrations of 3 units/ml and above. It is possible that the inability to neutralize heparin adequately in the TEG assay, may lead to falsely abnormal TEGs and cause treatment to be instituted when it is not warranted. Given these results, we should explore different delivery systems for heparinase such as the original heparinase bullet, which contains a higher concentration of heparinase. We are performing a current investigation comparing heparinase bullets to heparinase cups to determine which form of heparinase delivery is more capable of neutralizing large doses of heparin used during cardiopulmonary bypass.

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*Montefiore Medical Center; Montefiore Medical Center*

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Patients requiring cardiac surgery with CPB receive large doses of heparin that result in blood/plasma concentrations of approximately 2-5 IU heparin per ml. The heparinase cups neutralize this amount of heparin. We sought to determine whether the new TEG cups contain enough heparinase to neutralize the heparin in the blood of CPB patients.

**Method:** In a single-center, prospective, non-randomized, study, patients undergoing cardiac surgery had 10ml of blood collected prior to incision. A portion of that blood sample was used to run a baseline TEG using a plain cup and kaolin (360 mcl sample volume). We then took another portion of that blood sample and added incrementally increasing amounts of heparin in vitro to produce blood heparin concentrations of 2-8 IU/ml. These dilutions were performed in a 1000 mcl bullet by exchanging 3 mcl of whole blood for 3 mcl of the total heparin concentration needed to achieve our desired final concentration. The sample volume in the TEG was kept at 360 mcl for each assay. TEGs were performed on these samples using kaolin and heparinase cups to neutralize the heparin that was added in vitro.

**Statistics:** We used a paired t-test to compare difference in TEG R times between the baseline and different heparin concentrations.

**Results:** We found that there was no significant difference in the TEG R value between the baseline sample (no heparin) and the blood samples with 2U/ml of heparin added to them ( $6.39 \pm 1.34$  vs.  $7.29 \pm 1.66$ ,  $p = .053$ ). However, there was a statistically significant difference in the R value between the baseline TEGs and all of the TEGs which had 3 - 8 IU/ml of heparin added to them. For example at 5 IU/ml, the R value was  $8.26 \pm 2.70$  vs.  $6.60 \pm 1.41$  at baseline,  $p = 0.0002$ . At 8 IU/ml of heparin, the R value is  $8.67 \pm 2.42$  vs.  $6.75 \pm 1.40$ ,  $p < 0.00002$ .

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## EARLY TRACHEOSTOMY AFTER CARDIAC SURGERY AND POSTOPERATIVE OUTCOMES

Jerath A; Djaiani G; Wasowicz M; Al Kemyani N; Carroll J; Cabrerizo-Sanchez R; Karski J

*Toronto General Hospital*

### Introduction

Tracheostomy is a commonly performed procedure to facilitate weaning in patients who require prolonged ventilation. Optimal timing for tracheostomy after cardiac surgery remains a subject of debate and continued investigation. A particular concern relates to the proximity of sternal wound and potential of sternal wound infection and dehiscence. The purpose of our study was to assess the benefits of an early tracheostomy in a cardiac surgical population.

### Methods

Following REB approval we performed analysis of prospectively collected cardiac anesthesia and intensive care unit (ICU) database of 139 patients who underwent a tracheostomy between 1999 and 2006 in postcardiac surgery ICU. Timing to tracheostomy, ICU and hospital length of stay (LOS), and tracheostomy complications were recorded in addition to patient characteristics, type of surgery and postoperative outcomes. Based on the timing of tracheostomy patients were classed into two groups: Early Tracheostomy Group([SPCHAR(1e)]7days), and Late Tracheostomy Group (>7days).

Parametric data is reflected as mean  $\pm$  SD. Time to tracheostomy is described as median[range]. Demographic data and surgical characteristics were compared between groups with the Chi-Square test dichotomous variables, and the t-test for continuous variables. ICU and hospital LOS were analysed with Mann-Whitney U test. A p value < 0.05 was considered significant. Statistical analysis was conducted with the MINITAB computer software.(MINITAB Inc, State College, PA, USA)

### Results

The median times to tracheostomy were 7[3 – 7] days and 13[8 – 26] days in the Early (n = 33) and Late (n = 106) Tracheostomy Groups, respectively. There was no significant difference with respect to demographic data, co-morbidity rates, and surgical characteristics between the two groups.(Table 1)

Early tracheostomy was associated with lower incidence of postoperative renal failure, and shorter ICU and hospital LOS.(Table 2)

### Discussion

Modern tertiary cardiac surgical centres are now being confronted with a more high-risk and elderly strata of patients undergoing complex cardiac surgery. Little data exists on whether early tracheostomy would be of particular benefit in this group of patients. The current study identified that early tracheostomy was associated with lower incidence of postoperative renal failure, and shorter ICU- and hospital LOS without any increase in the perceived risk of mediastinitis and sternal dehiscence.

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## EEG-SPECTRAL ENTROPY IN BISPECTRAL INDEX-GUIDED ANESTHESIA DURING CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS.

Musialowicz T; Lahtinen P; Pitkänen O; Kurola J; Parviainen I

*Kuopio University Hospital*

**Background:** The spectral entropy of the EEG is a novel technique for monitoring anesthetic depth. In this entropy monitor, two parameters are calculated: state entropy (SE) which reflects the hypnotic level of anesthesia and is correlated with the bispectral index (BIS) values and response entropy (RE) which includes EEG and electromyographic components. The difference between RE and SE is an indicator of upper facial muscle activity, for example reflecting changes in responses to arousal reactions evoked by painful stimuli. The monitoring of anesthesia depth during cardiac surgery faces special challenges; in particular cardiopulmonary bypass (CPB) and hypothermia may induce changes in the EEG and in the level of hypnosis. Since the Bispectral Index (BIS) and entropy modules use different algorithms to measure the depth of anesthesia, we hypothesized that they may indicate different levels of the hypnotic component of anesthesia during cardiac surgery. The second hypothesis was that the RE would reflect better the responses to surgical stimulation than BIS and SE.

**Methods:** 32 patients scheduled to undergo elective cardiac surgery were included in this study. CPB with mild hypothermia (34°C) and anesthesia were standardised. SE, RE and BIS were recorded at the same time. BIS was maintained below 50 during anesthesia (propofol) and muscle relaxation according to train of four between 1-2. BIS, SE, RE and hemodynamic variables were also obtained one minute prior to and after the following events(see table 1). On the first and third postoperative day, patients were interviewed for evaluation of awareness during anesthesia. The paired T-test, and Pearson correlation coefficient were used for statistic analysis.

**Results:** The overall correlation during anesthesia between BIS (37±4) and SE (35±6; r2=0.9) and RE (37±6; r2=1.0) was very good, but there were significant differences between BIS and SE (7±5 ; range 1-20) and BIS and RE (5±4; range 1-20) in the different time points of anesthesia and surgery (Table 1). The RE-SE difference were significantly increased after skin incision(1±1&#8594;3±2)and sternotomy (2±1&#8594;3±2) but also BIS, SE and SAP were increased(p=0.05). No patient reported any recall of intraoperative events.

**Conclusion:** We noted a good overall correlation between BIS and spectral entropy during anesthesia in patients undergoing cardiac surgery. In contrast, though there were significant differences between the indices in the critical time points of anesthesia and surgery, these differences were sometimes almost 20 units. The RE was not any better than BIS and SE at predicting arousal after surgical stimulation.

## EFFECT OF CARDIOPULMONARY BYPASS AND HEPARIN ON PLATELET ACTIVATION MARKER- PLATELET FACTOR 4 (PF4) IN PEDIATRIC CARDIAC PATIENTS.

Sharma A; Suh A; Chen J

*Weill Cornell Medical College*

Objective: Contact between blood and the synthetic surfaces of a cardiopulmonary Bypass (CPB) circuit leads to platelet activation, and resultant platelet dysfunction contributes to postoperative bleeding. Platelet factor 4 (PF4), high-affinity heparin-binding protein, is produced in megakaryocytes and stored in platelet alpha granules and released upon activation. Primary function of platelet factor 4 is to neutralize the anticoagulant effect of heparin. We aimed to determine if there was a correlation between

1. Levels of PF4 pre and post CPB
2. Amount of heparin and difference in levels of PF4 pre and post CPB.
3. Length of CPB and difference in levels of PF4 pre and post CPB.

Methods: Ten patients between the ages of newborn to 6 years, undergoing open heart surgery involving cardiopulmonary bypass were included in the study after IRB approval. The blood samples were collected from the intra arterial catheter in CTAD tubes at two points- after induction of anesthesia and at the end of CPB. The quantitative determination of PF4 levels was performed by a highly sensitive Enzyme-Linked Immuno Sorbent Assay, according to manufactures instructions. Data was analyzed by ANOVA and comparisons were performed using paired t-tests and linear regression.

Results: Levels of PF4 increased in eight patients after CPB. Levels of PF4 ranged from 14.34-190.1 ng/ml pre CPB. Mean value 90.24 ng/ml. The levels post CPB ranged from 81.28- 205.7 ng/ml. Mean value 142.95 ng/ml. The increases in post CPB PF4 levels were statistically significant,  $p=0.01$ . There is no statistically significant correlation between amount of Heparin and change in PF4 level. There is no statistically significant correlation between length of CPB and change in PF4 levels.

There is a statistically significant correlation between pre CPB PF4 levels and difference in PF4 level pre and post CPB,  $p=0.004$ . Children with higher levels of PF4 pre CPB had smaller PF4 difference between pre and post CPB levels.

Conclusion: There is platelet activation during CPB which results in increase in PF4 levels. The increase in PF4 levels has no correlation to amount of heparin given during CPB or duration of CPB. There is an inverse correlation between pre CPB PF4 levels and PF4 difference pre and post CPB. Higher levels of PF4 pre CPB may be due to activated state of platelets in the pre-operative period. The difference between pre and post CPB PF4 may be less in patients with high pre CPB PF4 levels due to ceiling effect on amount of PF4 released by platelets on activation.

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## EFFECT OF DEXTROSE-BASED CARDIOPLEGIA DOSE ON INTRAOPERATIVE HYPERGLYCEMIA DURING CORONARY ARTERY BYPASS GRAFTING.

Baudo A; Hanni K; Soong W

*McGaw Medical Center of Northwestern University; Northwestern University*

**Introduction:** Perioperative hyperglycemia has consistently been linked to worsened postoperative outcomes, particularly in patients with diabetes undergoing cardiac surgery. Several potential factors have been identified as contributing to the hyperglycemic response to cardiopulmonary bypass (CPB). One intuitively obvious yet poorly studied etiologic factor is the use of dextrose-based cardioplegia solution. We performed a retrospective cohort study examining cardioplegia administration and degree of intraoperative hyperglycemia, expecting to find a somewhat linear relationship between dextrose dose and peak blood glucose level.

**Methods:** After IRB approval, we identified 84 consecutive patients who had undergone coronary artery bypass grafting (CABG) requiring CPB at our institution between October 2005 and July 2006. Subjects were excluded if the operative procedure had involved more than CABG (i.e., valve repair, aortic reconstruction, etc.). Data were collected on total intraoperative cardioplegia administered and peak blood glucose levels, as well as other variables previously reported. Linear regression analysis was used to plot peak blood glucose versus total dextrose administered, further stratified into groups of patients with or without a previous diagnosis of diabetes mellitus.

**Results:** There was no significant difference between the groups in terms of age or sex. In both diabetics and nondiabetics, there was a poor linear correlation between total dextrose dose and peak blood glucose levels (Figure,  $R^2 = 0.1567$  and  $0.1093$ , respectively). However, both groups demonstrated a significant deviation from null slope ( $P = 0.0335$  and  $0.0137$ , respectively). Additionally, there was no significant difference between the slopes of the two plots ( $P = 0.7922$ ).

**Discussion:** Only one trial in the extant literature directly examines the effect of dextrose-based cardioplegia solution on blood glucose levels. Intuitively, a direct relationship should exist between dextrose administration and degree of hyperglycemia. Although poorly linear, our data support the presumptive effect of dextrose-based cardioplegia on peak blood glucose levels. While there was no significant difference between the slopes plotted for diabetic versus nondiabetic patients, there was a trend toward more elevated glucose levels in diabetics than nondiabetics at higher dextrose doses. Our results are confounded by a previously presented significant difference in insulin administration between the two groups. Also, the relationship between total cardioplegia dose and duration of cardiopulmonary bypass has not been examined. Given the overwhelming evidence demonstrating the ill effects of hyperglycemia on perioperative outcomes in cardiac surgery, although more conclusive prospective trials are necessary, our data highlight the need to reassess the benefits and risks of dextrose-based cardioplegia.

## EFFECT OF PLATELET COUNT ON ARACHIDONIC ACID INDUCED PLATELET AGGREGATION IN PATIENTS UNDERGOING VASCULAR SURGERY

Thomson E; Nimmo A; Moores C; Beattie C; Thomson A

*The Royal Infirmary Of Edinburgh*

**Introduction:** The Multiplate® analyser (Dynabyte GmbH, Munich Germany) uses whole blood aggregometry to assess platelet aggregation in response to different agonists. The ASPI test measures platelet aggregation induced by arachidonic acid. This ASPI test reliably detects aspirin mediated platelet inhibition[1]. ASPI response has been shown to vary with platelet count in sequentially diluted whole blood samples from healthy volunteers[2]. It is not known whether the ASPI response in patients undergoing surgery is related to platelet count.

**Method:** Following regional ethics committee approval we prospectively studied patients presenting for elective vascular surgery who were receiving aspirin therapy. Blood was sampled before, during and after surgery for the Multiplate ASPI test and for laboratory measurement of platelet count (Sysmex XE-2100 analyser, TOA Medical Electronics, Kobe, Japan) ASPI responses are expressed as area under curve of impedance against time (AUC). ASPI response was plotted against platelet count. Data were analysed using linear regression models and Pearson correlation co-efficient.

**Results:** 39 patients were recruited who had received 75mg aspirin daily for at least one week before surgery and continued until the time of surgery. Operative duration ranged from 120 to 875 minutes. Blood loss ranged from 100 to 52200ml. The aggregation measured by the ASPI test correlated significantly with platelet count during and after surgery. The same relationship existed between ASPI response and platelet count in the samples taken before surgery as it did in those taken during and after surgery.

**Conclusions:** Platelet aggregation response in the ASPI test is correlated to the platelet count in patients on aspirin therapy having vascular surgery.

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## EFFECT OF PLATELET COUNT ON THROMBIN RECEPTOR ACTIVATING PEPTIDE INDUCED PLATELET AGGREGATION IN PATIENTS UNDERGOING VASCULAR SURGERY

Thomson E; Nimmo A; Moores C; Beattie C; Thomson A

*The Royal Infirmary Of Edinburgh*

Introduction: The Multiplate® analyser (Dynabyte GmbH, Munich, Germany) uses whole blood impedance aggregometry to assess in vitro platelet aggregation induced by a variety of agonists. Thrombin receptor activating peptide (TRAP) induces aggregation by activation of the thrombin receptor. The response measured to TRAP is little affected by aspirin[1] or clopidogrel[2]. The TRAP response has been shown to vary with platelet count in sequentially diluted whole blood samples from healthy volunteers[3]. We assessed the relationship between TRAP response and platelet count in patients having elective vascular surgery.

Method: With regional ethics committee approval, blood was sampled before, during and after surgery. Platelet aggregation following TRAP administration was measured using the Multiplate analyser and platelet count by laboratory analyser (Sysmex XE-2100, TOA Medical Electronics, Kobe). Data were analysed using non-linear regression. TRAP responses are expressed as area under curve of impedance against time (AUC). TRAP response expressed as a percentage of maximal TRAP AUC (TRAPmax) has been plotted against platelet count.

Data: 50 patients were recruited. 33 patients were taking daily aspirin 75mg until day of surgery, 4 patients clopidogrel 75mg, 6 patients both aspirin and clopidogrel. 7 patients had been on no anti-platelet therapy for >1 week prior to surgery. Operation time ranged from 120 to 875 minutes. Blood loss ranged from 100 to 52200ml. TRAP response varies with platelet count. This relationship is almost linear although appears to become less strong at high platelet counts

Conclusions: A correlation exists between TRAP response and platelet count in patients undergoing vascular surgery.

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## EFFECT OF VASOPRESSIN ON SURVIVAL OF PURKINJE NEURONS IN AN IN VITRO SIMULATED ISCHEMIA MODEL OF RAT CEREBELLAR SLICES

KIM H

*Seoul National University College of Medicine*

### Background

Arginine vasopressin (AVP) is frequently used in patients under the risk of brain injury. It has been shown to induce brain injury after ischemia and reperfusion in in vivo animal models. We determined the effect of vasopressin on the brain injury after ischemia-reperfusion using in vitro model.

### Methods

Cerebellar brain slices were prepared from adult Sprague-Dawley rats. They were then subjected to simulated ischemia (oxygen-glucose deprivation) for 20 min in the absence (control) or presence of vasopressin (5, 10, 50, 100, 500 pg/ml). After being recovered in oxygenated artificial cerebrospinal fluid for 5 h, they were fixed for morphologic examination to determine the percentage of live Purkinje cells.

### Results

There were no differences in the survival rate of Purkinje cells among the control and vasopressin groups.

### Conclusions

Vasopressin at concentrations studied has no direct effect on brain ischemia-reperfusion injury.

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## ELEVATED PREOPERATIVE HBA1C IN NON-DIABETIC PATIENTS PREDICTS POSTOPERATIVE HYPERGLYCEMIA AND PROLONGED ICU AND HOSPITAL LENGTH OF STAY AFTER CARDIAC SURGERY

Wagener G; Moitra V; Minhaz M; Mattis F; Lee H; Sladen R

*Columbia University*

Elevated Preoperative HbA1c in Non-Diabetic Patients Predicts Postoperative Hyperglycemia and Prolonged ICU and Hospital Length of Stay after Cardiac Surgery

### Introduction:

Patients with poor control of diabetes are at markedly increased risk of complications after cardiac surgery. The percentage of glycosylated hemoglobin (HbA1c) formed by exposure of Hb to plasma glucose is a routine measure of assessment of the efficacy of glucose control. We hypothesized that an elevated preoperative HbA1c may be a marker of poor glucose control even in patients without a history of diabetes undergoing cardiac surgery.

### Methods:

HbA1c was measured prior to cardiac surgery in 257 patients; an elevated level was defined as > 6.5%. Patients were considered non-diabetic if they took no anti-hyperglycemic medications and had no indication of diabetes in their chart. Postoperative hyperglycemia was defined as any blood glucose > 200 mg/dL on postoperative day (POD) 0 and 1. We noted ICU and hospital length of stay (LOS).

### Results:

An elevated HbA1c without a history of diabetes occurred in 36 patients (14.0% of the total). On POD 0 and 1, a significantly greater proportion of these patients had hyperglycemia compared to non-diabetic patients with normal HbA1c (POD 0: 80.6% vs. 53.0%,  $p < 0.001$ ; POD 1: 36.1% vs. 20.7%,  $p = 0.04$  by Chi-square). These patients also had a significantly longer ICU LOS (6.6 +/- 1.7 versus 2.5 +/- 0.3 days,  $p < 0.001$ ) and hospital LOS (13.5 +/- 2.2 versus 8.7 +/- 0.6 days,  $p = 0.003$ ; Figure). Using a linear regression model we found that the prolonged ICU and hospital LOS was independent of possible confounders (Parsonnet score, ejection fraction, age) and postoperative hyperglycemia ( $p = 0.003$  and  $p = 0.03$  respectively).

### Discussion:

Preoperative elevation of HbA1c in "non-diabetic" patients undergoing cardiac surgery is associated with increased postoperative hyperglycemia and prolonged ICU and hospital LOS. Our data suggest that HbA1c should become part of routine preoperative screening before cardiac surgery, and elevated HbA1c anticipates the need for close postoperative glycemic control. Our observation that prolonged LOS occurs in these patients even without postoperative hyperglycemia strongly suggests that this group may represent latent diabetics who require more extensive workup prior to elective surgery.

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# ENDOVASCULAR CORONARY SINUS CATHETER UTILIZATION IN MINIMALLY INVASIVE CARDIAC SURGERY

Lebon J; Couture P; Pellerin M; Bouchard D; Jeanmart H; Gevry Y; Rochon A; Aubé N; Laliberté É

*Montreal Heart Institute*

## Introduction

An endovascular coronary sinus catheter is installed in our institution to enable the administration of retrograde cardioplegia during minimally invasive cardiac procedures using Port Access technology. This is not an absolute indication as cardioplegia can be administered by the distal port of the aortic balloon. However, administration of retrograde cardioplegia remains interesting, if not necessary, in certain patients to obtain asystoly. Nevertheless, difficult positioning technique, coronary sinus perforation risks and high rate of displacement accounts for its lack of popularity. We reviewed our experience from the beginning of our minimally invasive cardiac surgery program to determine the safety and efficacy of a protocolized approach to the utilization of an endovascular coronary sinus catheter.

## Method

After approval from the Institution Review Board, we revised the files for the patients admitted for a minimally invasive cardiac surgery since 2006. A protocol was rigorously followed for the insertion and positioning of the endovascular coronary sinus catheter (Fig 1 and 2). Correct final position was accepted by the surgeon and the anaesthesiologist. Clinical success was defined jointly by the capacity of building a coronary sinus pressure greater than 30 mmHg during cardioplegia infusion and asystoly.

## Results

Data was collected from 61 files. A total of 59 endovascular coronary sinus catheters were installed (96.7%). The mean time to insert the catheter in the sinus ostium was 5.2 minutes. Only 13 % of the insertions took more than 10 minutes. Confirmation of an adequate position with fluoroscopy took an average of 9.2 minutes for a mean total procedure time of 15.5 minutes. Ventricularization of the coronary sinus pressure curve was observed in 83.6% of cases. The presence or absence of ventricularization was linked with clinical success in respectively 92.2% and 50.0% of cases ( $p = 0.0039$ ). No complications were documented secondary to sinus catheter installation. Time to insertion and total time were not associated with clinical success.

## Discussion

Endovascular coronary sinus catheter installation can be done in an acceptable time frame with a high rate of clinical success and without complications. During positioning, obtaining ventricularization contrary to time is related to the success rate.

## ENHANCED PLASMA MICROPARTICLE TISSUE FACTOR ACTIVITY IN PATIENTS DURING CARDIOPULMONARY BYPASS

Manly D; Mackman N; Welsby I

*Duke University Medical Center; University of North Carolina at Chapel Hill*

### Introduction

Despite anticoagulation with heparin during cardiopulmonary bypass (CPB), blood contact with the pericardial cavity and the heart-lung machine induce coagulation activation, release of inflammatory cytokines and hemolysis which may lead to microparticle (MPs) generation from activated leukocytes, red blood cells and platelets [1-2]. These MPs may be procoagulant, therefore we examined microparticle (MP) tissue factor (TF) activity in pericardial blood from patients undergoing elective cardiac surgery.

### Methods

Following IRB approval, blood was drawn from 10 patients within 20 minutes of the beginning and end of CPB and centrifuged into platelet-poor plasma (PPP). MPs were isolated from PPP and analyzed for tissue factor (TF) activity. Negative controls were venous samples from volunteers, positive controls were lipopolysaccharide (LPS) stimulated volunteer blood and blood aspirated from the pericardial cavity.

MPs were isolated from PPP by centrifugation as recently described [3] and incubated with either an inhibitory anti-human TF monoclonal antibody or a control mouse IgG. Next, human FVIIa and FX was added to each sample and incubated at 37 °C for 2 h. FXa generation was stopped by the addition of 25 μL of 25 mM EDTA buffer. The chromogenic substrate S2765 (4 mM) was added to each sample, incubated for 15 min at 37 °C and absorbance measured at 405 nm using a VERSAmax microplate reader (Molecular Devices). TF activity was calculated by reference to a standard curve using relipidated recombinant human TF (0-55 pg/mL). The TF-dependent FXa generation (pg/mL) was determined by subtracting the amount of FXa generated in the presence of HTF1 from the amount of FXa generated in the presence of the control antibody.

### Results

The baseline MP TF activity in venous blood from healthy individuals with our assay was  $0.1 \pm 0.3$  pg/ml. The MP TF activity in the LPS-positive control was  $3 \pm 5$  pg/ml and the MP TF activity in pericardial blood from patients during CPB was 18-fold higher,  $48 \pm 10$  pg/ml. We found that the average MP TF activity in blood extracted from the circuit pre-CPB was  $0.1 \pm 0.2$  pg/ml while the average MP TF activity in patients post-CPB was  $0.2 \pm 0.3$  pg/ml. Measurable MP TF activity was only observed in 20% of patients on CPB. MP TF activity of 11 and 4 pg/ml were noted in these patients. There was no difference between patients

### Conclusion

These data provide direct evidence that MP TF activity is enhanced only in a minority patients undergoing CPB. The mechanism of this activation is likely to be aspiration of activated pericardial blood into the cardiotomy reservoir. The role of the volume of pericardial aspirate and the association of MP TF with thrombotic outcomes after cardiac surgery will need to be examined in a larger patient group.

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## ERADICATING THE ANTI-ISCHEMIC OF BETA BLOCKERS: A METABOLIC PARADOX

Fontes M; Vladagina O; Franklin A; Chiu Y; Girardi L; Heerdt P

*Weill Medical College of Cornell University*

**Introduction:** The effects of beta-blockers (BB) on glucose homeostasis are complex – associated with both hypoglycemia in diabetics and hyperglycemia in nondiabetics. The latter may occur because of impaired glucose tolerance, worsening glycemic control, reduced insulin secretion in response to glucose, and impaired glucose uptake peripherally. Whereas hyperglycemia is common in the setting of cardiac surgery with use of cardiopulmonary bypass, little is known about glycemic control during CPB in nondiabetic patients treated with BB.

**Methods:** After approval by the Institutional Review Board, 120 non-diabetic adult patients with normal renal function undergoing elective cardiac surgery with use of hypothermic CPB were enrolled in this prospective and descriptive study. Comprehensive data on demographics, medical history, medications, laboratory values, and CPB related events were recorded. Serum glucose along with bladder temperature were measured after induction of anesthesia, at the onset of CPB, and then every 15 minutes until termination of CPB. Cardioplegia consisting of 4 parts blood and 1 part crystalloid including 5% dextrose was administered following cross clamping of the aorta. Hyperglycemia during CPB was defined as a plasma glucose value > 200 mg/dl. Univariate and multivariate analyses were performed to identify potential risk factors for CPB-related hyperglycemia. Only those predictors showing a two-tailed nominal P value of < 0.2 in univariate analyses were entered into stepwise multiple logistic regression analysis. P value of less than 0.05 was considered significant. Lastly, the predictor variables including surgical characteristics were compared between patients preoperatively treated with BB and patients not treated (NBB).

**Results:** As a population, the mean baseline glucose was consistent with a non-diabetic state; however; the BB group had a significantly higher baseline glucose as compared to the NBB group (Table 1). The BB and NBB groups also differed by weight and by procedure with a higher proportion of patients undergoing CABG surgery being on BB. In both groups, the mean plasma glucose during CPB was significantly elevated (BB: 224 + 42 mg/dl and NBB: 219 + 35 mg/dl; relative to baseline). According to multivariate analysis, both preoperative treatments with BB (OR: 2.89; p=0.0152) and the amount of cardioplegia administered (OR: 4.15; p=0.0015) were independent predictors of hyperglycemia.

**Conclusion:** Our findings in this preliminary study raise concern about BB therapy in nondiabetic patients undergoing CPB. The associated hyperglycemia and its relation to postoperative vascular outcomes warrant further investigation.

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## FEASIBILITY OF THREE DIMENSIONAL TRANSESOPHAGEAL ECHOCARDIOGRAPHY FOR ANATOMICAL DEFINITION AND CATHETER GUIDANCE DURING ELECTROPHYSIOLOGY ABLATION

Mahajan A; Ho J; Swenson S; Nakahara S; Corniea J; Shivkumar K

*David Geffen School of Medicine at UCLA*

**Background:** Many common chronic cardiac arrhythmias require transeptal placement of left atrial catheters for electrophysiology (EP) study and ablation. The anatomy of this chamber is complex and variable and must be accurately assessed to appropriately and safely ablate the source of the arrhythmia percutaneously. Currently, three dimensional (3D) mapping is achieved via the EnSite NavX system, using the patient's pre-acquired computed tomography (CT) image correlated with electroanatomic mapping. However, it does not provide real time imaging of anatomic structures and the process is time consuming, costly and involves further exposure to radiation. With the introduction of echocardiographic systems capable of real time transesophageal 3D imaging, transesophageal echocardiography (TEE) may provide a superior means of facilitating these procedures. We investigate the feasibility of using live and full-volume 3D TEE during left atrial EP procedures.

**Methods:** After Institutional Review Board approval with waiver of consent, consecutive patients requiring TEE evaluation to rule out intra-cardiac clots prior to left sided EP ablations were studied. EKG gated full volume and live 3D images of the left atrium were acquired, attempting to identify 8 left atrial structures of interest to the EP interventionalist (pulmonary veins x4, left atrial appendage, mitral isthmus, lateral mitral annulus, left atrial fossa). Critical points of the procedure were visualized in real time.

**Results:** Six patients were studied. 83% of structures were visualized. EKG gated full volume 3D images were suboptimal in 3/6 patients due to irregular cardiac rhythm. In these patients live 3D was able to visualize 83% percent of structures of interest. Transeptal puncture was visualized in 100% of patients (fig 1). The TEE probe did not interfere with fluoroscopic visualization of structures. Live 3D monitoring of catheter position and tissue contact was performed during ablation in all patients (fig 2). No complications occurred due to the TEE or ablation procedure in these six patients.

**Conclusions:** This study demonstrates the feasibility of EKG gated and live 3D imaging in left sided electrophysiology ablations to define left atrial anatomy and visualize ablation catheter location in real time. Subjectively, real time 3D imaging provides the interventionalist a dramatic improvement in confidence of catheter location during ablation with potential improvement in safety. The high incidence of irregular cardiac rhythms diminishes the role of EKG gated full volume imaging; live 3D is capable of identifying anatomy and catheter position during these procedures.

## FONDAPARINUX AND BIVALIRUDIN PRODUCE A SYNERGISTIC EFFECT ON ANTICOAGULATION AS MEASURED BY THROMBOELASTOGRAM

Zanghi C; Eaton M

*University of Rochester Medical Center*

Since its inception, cardiopulmonary bypass (CPB) has relied on systemic anticoagulation with unfractionated heparin. Heparin with protamine provides a rapid reversal mechanism and half a century of documented clinical experience. Heparin also presents potential complications including infectious risks, inter-patient variability, and significant immunogenicity. The direct thrombin inhibitor (DTI) bivalirudin has been evaluated as a substitute for heparin during CPB, especially in patients suffering from Heparin Induced Thrombocytopenia (HIT). Three prospective studies have attempted to evaluate the efficacy of bivalirudin in place of heparin during CPB. All 3 trials showed similar clinical outcomes when heparin and bivalirudin were compared [1,2,3]. Despite these results, it also has significant limitations. The rapid proteolytic degradation of bivalirudin can result in clearance of the drug from the circuit during periods of stasis, resulting in clot formation [3]. In addition, a study comparing DTIs with heparin showed that DTIs lengthen the time needed for clot formation, but they have little to no effect on clot propagation and strength [4]. Fondaparinux, a synthetic anticoagulant, has the potential to attenuate clot propagation and strength, without inducing HIT, but is not currently approved for CPB [4,5]. The effects of fondaparinux and bivalirudin in human blood alone and in combination, were assessed in vitro using thromboelastogram (TEG). The combination resulted in a statistically significant increase in the R time, as compared to the effect of either drug alone ( $P < 0.05$ , 1-way ANOVA with Bonferroni's multiple comparisons test) (see table). TEG tracings of the drug combination also demonstrated profound global anticoagulation, which was absent from the tracings of either drug alone. Thus, we present preliminary evidence that combination therapy with bivalirudin and fondaparinux may be more effective than bivalirudin alone during bypass.

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## HAEMODYNAMIC RESPONSES TO DIRECT CONVENTIONAL VS. VIDEO LARYNGOSCOPY IN PATIENTS WITH CORONARY ARTERY DISEASE

Kanchi M; Nair H

*Narayana Hrudayalaya*

### Introduction:

Tracheal intubation is associated with sympathetic stimulation and increase in heart rate and blood pressure, which may predispose patients with coronary artery disease to myocardial ischaemia. The aim of the study was to compare the haemodynamic changes using a video laryngoscope (Pentax) with that of conventional laryngoscopy and endotracheal intubation.

### Methods:

After IRB approval and informed consent, 30 patients scheduled for elective coronary artery bypass grafting were randomly allocated to two groups. In-group –A video laryngoscope (Pentax) was used to aid endotracheal intubation, which in group-B, conventional laryngoscopy and endotracheal intubation was performed by an experienced anaesthesiologist. Patients with poor left ventricular function and left main disease were excluded from the study. Anaesthesia was induced with fentanyl, midazolam and endotracheal intubation performed after pancuronium. Anaesthesia was maintained with isoflurane in oxygen, fentanyl and midazolam. Haemodynamic data were recorded at specific intervals and statistically analysed.

### Results:

There were 30 patients: 15 in each group. No significant differences in the demographic data (Table-I). The duration of laryngoscopy and intubation was significantly increased in group-A (video laryngoscope) when compared to group-B (conventional laryngoscope). The haemodynamic changes are mentioned in Table-II. There were no significant differences in the haemodynamic data (similar changes were seen in either groups).

### Conclusion:

The Pentax – AWS video laryngoscope is commercially available and this study did not demonstrate benefit in terms of haemodynamic changes due to laryngoscopy and endotracheal intubation in patients undergoing elective CABG. There have been several reports of its successful use in patients with difficult airway, if Pentax – AWS is beneficial in patients with coronary artery disease with difficult airway, is to be studied in these subset of population.

## HEMOFILTRATION DURING CARDIOPULMONARY BYPASS DOES NOT DECREASE THE INCIDENCE OF ATRIAL FIBRILLATION AFTER CARDIAC SURGERY

Mauermann W; Andrew H; Nuttall G; Oliver W

*Mayo Clinic Rochester*

**INTRODUCTION:** Atrial fibrillation (AF) occurs in 20% to 50% of patients after cardiac surgery (1,2). AF after cardiac surgery is associated with the need for additional treatment and prolonged hospital stays. Two randomized trials have demonstrated that perioperative therapy with corticosteroids is effective in decreasing the incidence of postoperative AF, presumably by attenuating the inflammatory response to surgery and cardiopulmonary bypass (CPB) (1,2). Hemofiltration during CPB has also been reported to decrease the quantity of inflammatory mediators (3). We hypothesized that hemofiltration during CPB may also be beneficial in decreasing the incidence of AF after cardiac surgery.

**MATERIALS AND METHODS:** This was a retrospective review of patients previously enrolled in a double-blinded, randomized, placebo controlled trial. The original trial has been previously published (4). 192 patients undergoing cardiac surgery were randomized to Group Control (saline), Group Hemofil (hemofiltration during CPB until 27 ml/kg of ultrafiltrate was obtained), or Group Steroid (1 g methylprednisolone intravenously before surgery and 4 mg of dexamethasone every 6 hours for the subsequent 24 hours). A blinded reviewer retrospectively reviewed all patient records to determine the incidence of new onset AF in each study group. AF was considered to have occurred if there was any ECG evidence of AF or if it was mentioned in any daily progress note or the discharge summary.

**RESULTS:** The data from 185 patients from the original study were available for this review. 92 patients underwent CABG (50%), 85 patients had a valve operation (46%), and 8 patients had a combined CABG / valve operation (4%). Sixty patients (32%) had new onset AF after cardiac surgery. There was no difference between groups in the incidence of AF (Group Control 21%, Group Steroid 41%, Group Hemofil 36%;  $p = 0.057$  between groups). The only significant risk factor for the development of AF was age (mean age of patients with AF was 65.4 +/- 10.1 years versus 61.4 +/- 11.5 years for no AF;  $p = 0.024$ ). When age was controlled for in multivariate analysis the difference between study groups remained non-significant ( $p = 0.067$ ).

**DISCUSSION:** In this group of patients hemofiltration showed no benefit in reducing the incidence of new onset AF after cardiac surgery. This is consistent with a previously performed retrospective study (3). Despite using doses of steroids similar to those in randomized trials, we found no benefit of perioperative corticosteroid therapy in reducing the incidence of AF. Our study was retrospective in nature and as such we likely captured only clinically significant episodes of AF that required treatment. The two positive randomized trials used continuous telemetry for either 84 hours (1) or 7 days (2). Thus, it may be that corticosteroids are effective in preventing transient, less clinically significant episodes of AF but not more persistent, clinically significant episodes.

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## HEPARIN CONCENTRATION BASED ANTICOAGULATION FOR CARDIAC SURGERY FAILS TO ACCURATELY PREDICT HEPARIN BOLUS DOSE REQUIREMENTS

Garvin S; Body S; Despotis G; Shekar P; Fitzgerald D

*Brigham and Women's Hospital; Washington University School of Medicine*

### Background:

Hemostasis management has evolved to include sophisticated point-of-care systems that provide individualized dosing through heparin concentration based anticoagulation. The Hepcon® HMS Plus system (Medtronic Inc., Minneapolis, MN) via Heparin Dose Response (HDR) estimates heparin dose, however, the accuracy of this test has not been systematically evaluated in large cohorts.

### Methods:

We examined institutional databases for all patients who underwent cardiac surgery with cardiopulmonary bypass (CPB) at our institution from February 2005 to July 2008. During this period, the Hepcon was used exclusively for assessment of heparin dosing and coagulation monitoring. Detailed demographic, surgical, laboratory and heparin dosing data were recorded. Activated clotting time (ACT), calculated and measured HDR and heparin concentrations were recorded. Performance of the Hepcon was assessed by comparison of actual and target ACT values and calculated and measured HDR.

### Results:

In 4105 patients undergoing cardiac surgery, heparin bolus dosing to a target ACT resulted in wide variation in the post-heparin ACT ( $r^2=0.03$ ). The post-heparin ACT did not reach the target ACT threshold in 7.5% (i.e., when target ACT was 300 seconds) and 13.8% (i.e., when target ACT was 350 seconds), of patients. Similarly, the target heparin level calculated from the HDR did not correlate with the post-bolus heparin level, with 18.5% of samples differing by more than two levels of the assay. Calculated and measured HDR were not linearly related at any heparin level ( $r^2 < 0.02$ ) (Figure 1).

### Conclusions:

Hepcon® HMS Plus system fails to provide clinically useful data for estimating heparin bolus dosing in the pre-CPB period and perhaps with respect to identifying patients with substantial heparin resistance. Further prospective studies are needed to elucidate what constitutes adequate anticoagulation for CPB and how clinicians can reliably and practically assess anticoagulation in the operating room.

## HEPARIN DOSE RESPONSE IS INDEPENDENT OF PREOPERATIVE ANTITHROMBIN ACTIVITY IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

Collard C; Garvin S; Fitzgerald D; Chen J; Muehlschlegel J; Perry T; Fox A; Shernan S; Body S

*Brigham and Women's Hospital; Saint Luke's Episcopal Hospital; Talecris Biotherapeutics, Inc.*

### Background:

The primary mechanism of action of heparin is to potentiate the enzymatic activity of antithrombin (AT). We hypothesized that there would be an association between preoperative AT activity and heparin-dose response (HDR) in patients undergoing cardiopulmonary bypass graft (CABG) surgery.

### Methods:

From 325 patients who underwent CABG from February 2005 to July 2007 at our institution, we collected demographic, pre-operative laboratory and operative data. AT activity was measured after induction of anesthesia using a colorimetric method (Siemens Healthcare Diagnostics, Tarrytown, NY). HDR was measured using Hepcon® HMS Plus system (Medtronic Inc., Minneapolis, MN) and calculated according to the formula: Calculated heparin dose response (secs/unit/mL) = (Target ACT – Baseline ACT) / Calculated Target Heparin Level. Multivariate linear regression modeling of HDR was performed to examine for predictors of HDR. Subgroup analysis of patients with low AT activity, who may be at risk for heparin resistance was also performed.

### Results:

Mean baseline ACT was  $135 \pm 18$  seconds. Mean calculated HDR was  $98.7 \pm 21.8$  seconds/unit/mL. Baseline AT activity was  $0.93 \pm 0.13$  units/ml. There was no correlation found between baseline AT activity and baseline ACT or post-heparin ACT. HDR was not associated with AT concentration, platelet count or elevated baseline PTT. AT activity was not predictive of HDR (Figure 1). Clinical predictors of HDR are listed (Figure 1). Addition of AT activity to the clinical multivariable model did not significantly improve model performance. Subgroup analysis of 53 patients with baseline AT < 80% of normal levels was performed, and did not show a relationship between AT activity and HDR.

**Conclusion:** Although potentiation of AT activity is the primary mechanism by which heparin facilitates anticoagulation for CPB, there does not appear to be a clinically evident relationship between AT activity and measured heparin-dose response.

## HIGH DOSE TRANEXAMIC ACID AND POSTOPERATIVE SEIZURES AFTER CARDIAC SURGERY

Jerath A; Gower S; Djaiani G; Tait G; Carroll J; Karski J; Fedorko L

*Toronto General Hospital*

### Introduction

Tranexamic acid (TA) has become the forefront antifibrinolytic drug in the perioperative management of cardiac surgical patients reducing blood loss and blood product transfusion rates. Although TA has an excellent safety profile, there is growing body of evidence that at high doses, it can induce seizure activity in the early postoperative period. The current study sought to determine if intraoperative administration of TA in excess of 100mg/kg could be a contributing factor to postoperative seizure activity after cardiac surgery.

### Methods

Following REB approval, we performed analysis of prospectively collected cardiac anesthesia and intensive care unit database of 142 consecutive patients undergoing cardiac surgery with cardiopulmonary bypass (CPB) over the two months period from December 2007 to January 2008 at our institution. TA was administered in all patients. Based on the intraoperative TA dosage, all patients were classed into two groups: High TA Group, and Low TA Group. High dose of TA was defined as the total intraoperative dose of TA  $\geq$  100mg/kg, and low dose as  $<$  100mg/kg.

Demographic data and surgical characteristics were compared between groups with the Chi-Square test for dichotomous variables, and the t-test for continuous variables. A p value  $<$  0.05 was considered significant. Statistical analysis was conducted with the MINITAB computer software.(MINITAB Inc, State College, PA, USA)

### Results

The median doses of TA were 109 mg/kg and 67 mg/kg in the high (n = 39) and low (n = 103) TA groups respectively. (Figure) Patients in the high TA group were more likely to have a history of congestive heart failure, higher blood product transfusion rates, and longer CPB time. (Table)

Postoperative seizure rates were 15.4% (95% CI 4% to 26.8%) in the high TA group versus 4.8% (95% CI 0.7% to 8.9%) in the low TA group, p=0.036

### Discussion

The TA dosage in excess of 100 mg/kg appears to be associated with seizure phenomenon after cardiac surgery. TA may induce seizure activity via its dose dependent antagonism of the central GABA<sub>A</sub> receptor. Further research is required to clarify if TA has a dose-dependent mechanism of postoperative seizure induction after cardiac surgery.

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## HOW MUCH FIBRINOGEN IS NECESSARY TO OPTIMIZE CLOT FORMATION AFTER HEMODILUTION?

Bolliger D; Szlam F; Molinaro R; Levy J; Tanaka K

*Emory University Hospital*

**Introduction:** Coagulopathy after cardiac surgery involves multiple elements, and low fibrinogen level is considered an important cause.<sup>[1]</sup> The critical fibrinogen level has been conventionally set at 100 mg/dL,<sup>[2]</sup> <sup>[3]</sup> but there is a paucity of information to support this recommendation. We hypothesize that the optimal fibrinogen level represents its plasma concentration at which the rate of clot formation becomes normalized in clotting blood after hemodilution. Thus, we utilized thromboelastometric techniques to model hemodilution and the effect of fibrinogen substitution.

**Methods:** After written informed consent, citrated blood was drawn from six healthy volunteers. Blood was diluted to 70% with natural saline and adjusted with allogeneic type-matched red blood cell concentrate to restore hematocrit to about 24%. Fibrinogen levels were determined to be  $384 \pm 75$  and  $70 \pm 11$  mg/dL before and after dilution, respectively. Aliquots of 1 mL diluted blood were incubated with 0, 0.5, 1, 1.5, 2, and 3 mg fibrinogen (Haemocomplettan<sup>[4]</sup> P, CSL Behring, Marburg, Germany). Thrombelastography using ROTEM<sup>[5]</sup> (Pentapharm, Munich, Germany) was performed, and the following parameters were collected: angle ( $\alpha$ , in degree) defined as angle between baseline and a tangent through the 2 mm point; clotting time (CT, in sec) defined as time from start to an amplitude of 2 mm; and maximal clotting formation (MCF, in mm) defined as the maximal amplitude of the tracing. All measurements were performed twice. Undiluted whole blood (WB) was used as control. With the values of  $\alpha$ , ED50 and ED90 were calculated using Hill's equation.

**Results:** As  $\alpha$  represents both velocity and magnitude of clot formation, our analyses were focussed on this parameter. Normal value for  $\alpha$  in WB was  $73 \pm 3$  degrees (range from 68 to 79 degrees). Substitution with fibrinogen increased  $\alpha$  in a sigmoid shape from  $42 \pm 6$  degrees after the dilution to  $78 \pm 4$  degrees after the highest substitution with 3 mg/mL fibrinogen ( $P < 0.001$  by ANOVA). Only after adding fibrinogen  $1.5$  mg/mL,  $\alpha$  was similar to control with WB. ED50 and ED90 were calculated to be 1.25 mg/mL and 1.82 mg/mL fibrinogen, respectively. Increasing fibrinogen levels also led to a dose-dependent improvement of CT and MCF ( $P < 0.001$  by ANOVA).

**Conclusion:** According to the current transfusion guidelines, the substitution of fibrinogen is recommendation for plasma levels below 80-100 mg/mL.<sup>[2]</sup> <sup>[3]</sup> However, our data suggest that the rate of clot formation is optimized only after increasing fibrinogen level to  $>200$  mg/mL.

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## HYPERGLYCEMIA-INDUCED ABOLISHMENT OF SEVOFLURANE POSTCONDITIONING PROTECTION OF THE DIABETIC RAT HEART IS NOT REVERSED BY INSULIN

Drenger B; Ostrovsky I; Barak M; Nechemia Y; Ziv E

*Hadassah University Hospital; Rambam Medical Center*

**Background:** Sevoflurane postconditioning (postC) may reduce infarct size when administered following myocardial ischemic insult. This effect may be blocked by hyperglycemia. The effectiveness of postC protection in animals with diabetes mellitus is unknown. We examined the role of mechanical (M) and sevoflurane (S-sevo) postC in streptozotocine-induced diabetic rats (D), and whether insulin would reverse the diabetic effect.

**Methods:** Acutely instrumented anesthetized diabetic (for 30 days) or non-diabetic rats were randomly subjected to a 30-min period of regional ischemia (left coronary artery temporary ligation) followed by 3 hours of reperfusion. Both groups were subjected to mechanical postC (three 2-min ischemia/reperfusion intervals on early reperfusion), or to 5 min 2.4% sevo postC, with and without KATP antagonist, 5-hydroxy decanoate sodium (5-HD) and PI3K antagonist wartmannin. The studies were repeated with insulin (I) given for 48 hours to the diabetic rats to ensure normoglycemia prior to the experiment. Area of infarction proportionate to the area-at-risk (TTC staining) and amount of apoptosis (TUNEL assay) were used in order to evaluate myocardial tissue salvage by postC. The Tukey's–Kramer Multiple Comparisons Test and Unpaired Student's t-test were used for the statistical analysis.

**Results:** Mechanical postC and sevo postC, both significantly reduced infarct size in the non-diabetic rats (from  $20\pm 1.5\%$  infarct size proportionate to the area at risk ( $n=12$ ) to  $11\pm 1.5$  and  $9.4\pm 3.1\%$ , ( $n=10$ ), respectively ( $p>0.001$ )). Hemodynamic parameters did not differ significantly between groups. Both 5-HD and wartmannin have completely reversed the postC effect in the two groups. Diabetes (blood glucose  $> 500$  mg/dl,  $n=8$  in each group) did not alter infarct size ( $18\pm 2.3\%$ ), but blocked the protective effects of both mechanical ( $19\pm 1.8\%$ ) and sevo postC ( $21\pm 1.2\%$ ). Normoglycemia by insulin ( $n=5$ ) did not reverse the unfavorable diabetic blockade of postC, on the contrary, a significant rise in infarct size was noted ( $p<0.0001$ ). TUNEL-positive cell count in mechanical and sevo postC groups was significantly lower than control ( $p<0.05$ ).

**Conclusions:** Our results demonstrate that both mechanical and sevo postC effectively reduce infarct size and apoptotic cell death (by about 50%) in non-diabetic rat hearts. These positive effects were completely abolished in severe hyperglycemic diabetic rats. However, restoring normoglycemia in these diabetic rats with insulin administration did not change the inhibitory effect of diabetes on postC hearts, indicating possible involvement of insulin in increasing myocardial metabolic requirements. Both KATP channels and the PI3K-Akt pathways seem to be involved in these protective effects of postC.

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## IMPACT OF THE KIMBERLY-CLARK PATIENT WARMING SYSTEM ON TEMPERATURE PERTURBATIONS FOLLOWING CARDIAC SURGERY WITH CARDIOPULMONARY BYPASS

Ju A; Arunajadai S; Rodriguez A; Shanewise J; Sladen R

*Columbia University*

**Introduction:** During the rewarming phase of cardiopulmonary bypass (CPB), cold peripheral tissues rewarm slowly and incompletely. After separation from CPB, core heat redistributes to peripheral tissues, leading to a 1-2°C "afterdrop" [1]. In the ICU, emergence from anesthesia is characterized by endogenous rewarming, vasodilation, hemodynamic instability, and increased oxygen consumption. The Kimberly-Clark Warming System (KCWS) is an FDA-approved device that uses temperature-regulated fluid flowing through adherent skin pads; it is able to decrease hypothermia during off-pump coronary revascularization [2]. Based on a retrospective analysis [3], we wished to test the hypothesis that use of the KCWS during CPB rewarming would decrease afterdrop and postoperative thermal flux.

**Methods:** After IRB approval, 43 patients undergoing CPB for cardiac surgery were recruited. Exclusion criteria included preoperative dialysis, absent pedal pulses, and hypothermic circulatory arrest. CPB was conducted at 32°C. All patients were rewarmed on CPB with blood heated to 37.5°C. 23 patients had external rewarming with the KCWS set to maintain a nasopharyngeal temperature of 37°C, while 20 patients (control group) received forced-air rewarming only. Both KCWS rewarming and forced-air rewarming were maintained until the patient left the OR. Afterdrop was measured as the decrease in pulmonary artery (PA) temperature from end-CPB to ICU arrival. In the ICU, staff and data collectors were blinded to assignment group, and all patients received forced-air rewarming until pulmonary artery (PA) temperature reached 37°C.

**Results:** No significant differences were found between KCWS and controls in afterdrop (0.62°C v 0.93°C,  $p=0.28$ ), the postoperative rewarming curves (Fig. 1), or areas under the curves of ICU rewarming (297.42 °C\*hr v. 296.85 °C\*hr,  $p=0.72$ ). However, the peak rate of ICU rewarming (Fig. 2) was less in the KC group. The 95% confidence intervals for the KC and control rewarming curves do not overlap between hours 2-7, implying a statistically significant decrease in rate of rewarming during that period.

**Discussion:** Although afterdrop was not decreased by use of the KCWS, the decrease in the rate and intensity of rewarming in the ICU suggests a potential benefit on postoperative thermal flux. We are currently examining the impact of this benefit on postoperative hemodynamics and oxygen consumption.

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## INCIDENCE OF HYPOPHOSPHATEMIA DURING CARDIOPULMONARY BYPASS

Shanks A; Caldwell M; Dorje P; Laura P

*University of Michigan*

**Background:** Hypophosphatemia is associated with adverse outcomes in surgical patients. Cardiac surgery involving cardiopulmonary bypass (CPB) places patients at risk of developing clinically significant hypophosphatemia secondary to hemodilution and hypothermia. The goal of this study was to determine the incidence of intraoperative moderate to severe hypophosphatemia in patients undergoing cardiac surgery with CPB. Hypophosphatemia at the time of separation from CPB may have important implications for cardiovascular function and cellular homeostasis.

**Methods:** This was a prospective observational study without intervention. We recruited 12 patients presenting for elective cardiac surgery to determine intraoperative serum phosphate levels. Clinicians were blinded to the test results and delivered customary perioperative care. Moderate hypophosphatemia was defined as serum phosphate level  $\geq 1.0$  mg/dL but  $< 2.5$  mg/dL. Severe hypophosphatemia was defined as serum phosphate level  $< 1.0$  mg/dL. Reference phosphate levels for our laboratory were 2.7mg/dL – 4.6mg/dL. Serum phosphate levels were determined at 5 time points:

- 1) Following induction of anesthesia but prior to heparin administration for CPB
- 2) Two minutes after instituting full CPB flow
- 3) Upon reaching the targeted hypothermic temperature
- 4) Following rewarming but prior to separation from CPB
- 5) Following reversal of heparin with protamine

**Results:** The incidence of moderate hypophosphatemia at the time of separation from CPB was 41.7%. Although only 16.7% of patients were found to have moderate hypophosphatemia at the time of initial blood draw, 91.7% developed moderate hypophosphatemia intraoperatively. Moderate hypophosphatemia was most prevalent immediately following the institution of CPB (63.6%). The lowest measured intraoperative phosphate level was 1.5mg/dL. No patients developed severe hypophosphatemia intraoperatively.

**Conclusion:** Although previous studies described hypophosphatemia in ICU patients following cardiac surgery, ours is the first to describe intraoperative hypophosphatemia. There is a high incidence of moderate hypophosphatemia at the time of separation from CPB, but the clinical significance is not known. Additional studies to further characterize phosphate disturbance and correction during the intraoperative period are needed. Clinicians should consider routine phosphate measurement and replacement in cardiac surgical patients.

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## INTRAOPERATIVE 3D TEE IDENTIFIES VARIATION IN MITRAL VALVE LEAFLET SEGMENTS DISPLAYED BY CONVENTIONAL 2D TEE IMAGING PLANES

Kwak J; Shernan S; Shook D

*Brigham and Women's Hospital, Harvard Medical School*

**Introduction:** ASE/SCA guidelines for performing a comprehensive two-dimensional (2D) transesophageal echocardiography (TEE) examination of the mitral valve (MV) are based on normal cardiac anatomy[1]. It is unclear how anatomic variation due to MV pathology affects MV leaflet segments displayed by these 2D planes. We aimed to determine the variation in MV leaflet segments identified by conventional 2D TEE imaging planes using real-time three-dimensional fully-sampled matrix array TEE (RT3D-MTEE) for comparison.

**Methods:** Cardiac surgery patients with at least moderate mitral regurgitation (MR) undergoing clinically-indicated intraoperative RT3D-MTEE (iE33; Philips Healthcare, Inc.) were prospectively included in the study. Cardiac anesthesiologists certified in perioperative TEE reviewed the ASE/SCA guidelines for MV examination and obtained the following midesophageal (ME) 2D images, each with concurrent, corresponding live RT3D-MTEE images: four chamber (4C), mitral commissural (MC), two chamber (2C), and long axis (LAX). MV leaflet segments expected to be visualized in the 2D imaging planes according to ASE/SCA guidelines were compared to actual leaflet segments displayed by corresponding live RT3D-MTEE images.

**Results:** Eight cardiac surgical patients with MV pathology, including leaflet prolapse or flail (N= 7) or functional MR (N= 1), were analyzed. Using RT3D-MTEE for validation, expected MV leaflet segments were correctly displayed in 88% of MC views and 88% of 2C views. However, expected MV leaflet segments were correctly displayed in only 13% of 4C views (Figure 1) and 38% of LAX views (Figure 2).

**Conclusion:** In comparison to conventional 2D TEE, RT3D-MTEE may more accurately identify MV leaflet segments in patients with pathology. Further investigation is warranted to determine the utility of RT3D-MTEE in perioperative clinical decision-making for patients with MV disease.

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Figure 1. Conventional 2D ME 4C image (A) and corresponding live RT3D-MTEE image (B) showing discrepancies between expected and actual MV leaflet segments displayed. The ME 4C view consistently displayed the A2 and P2 leaflet tips rather than the expected A1 and P1 leaflet tips. There was considerable variation in the anterior leaflet body segment and leaflet tips displayed in each ME 4C view.

Figure 2. Conventional 2D ME LAX image (A) and corresponding live RT3D-MTEE image (B) showing discrepancies between expected and actual MV leaflet segments displayed. According to live RT3D-MTEE images, 2D ME LAX views displayed the A3 and P3 leaflet tips and A3 body rather than the expected A2 and P2 leaflet tip and A2 body.

## INTRAOPERATIVE HYPERGLYCEMIA EXACERBATES POSTOPERATIVE MYOCARDIAL INJURY FOLLOWING CARDIAC SURGERY

Pabich W; White W; Podgoreanu M; Smith M; Mathew J

*Duke University*

### INTRODUCTION:

Hyperglycemia is a predictor of mortality in patients hospitalized with acute coronary syndrome (ACS).(1) Strong evidence links perioperative hyperglycemia to reduced survival and postoperative morbidity following cardiac surgery.(2) However, the role of intraoperative glycemic control is comparatively poorly defined and controversial.(3) Furthermore, while preclinical studies indicate a direct relationship between hyperglycemia and myocardial infarct size, the association between intraoperative hyperglycemia and extent of myocardial ischemia-reperfusion injury associated with cardiac surgery has not been reported. We hypothesized that acute intraoperative hyperglycemia, defined as the amount of time spent above normoglycemic levels (>8mmol/L or 144mg/dL), exacerbates the severity of perioperative myocardial injury (PMI).

### METHODS:

With IRB approval we conducted a retrospective analysis of adult patients undergoing elective CABG or CABG/valve surgery at a single university center (n=205). PMI was assessed using plasma levels of cardiac troponin I (cTnI) on postoperative day one (Siemens, upper limit of normal 1.5 ng/mL). Serial intraoperative whole blood glucose values were electronically recorded. Insulin management was at the discretion of the anesthesia team; GIK infusions are not routinely employed at our institution. Multiple linear regression was used to test the relationship between cTnI, intraoperative hyperglycemia (time spent >8mmol/L), diabetic status, aortic cross-clamp time, preoperative ejection fraction, and indexed intraoperative insulin (total insulin dose/surgical time), along with their 2-way interactions. Age, CPB time, and Parsonnet risk index were tested, but found to be not significant.

### RESULTS:

PMI severity significantly associated with duration of intraoperative hyperglycemia and further worsened by longer aortic cross-clamp times ( $p < 0.001$ , Figure 1). Interestingly, non-diabetics (66.2%) experienced increased PMI with intraoperative hyperglycemia and longer cross-clamp times compared to known diabetic patients ( $p=0.004$ ). However, LV dysfunction in diabetics was associated with PMI ( $p=0.02$ ). Indexed intraoperative insulin was not independently associated with PMI, but only in interaction with intraoperative hyperglycemia ( $p=0.05$ ). The overall model  $r^2$  was 0.27 ( $p<0.0001$ )

### CONCLUSION:

Intraoperative hyperglycemia in interaction with ischemic time, diabetic status and LV dysfunction exacerbates severity of PMI in cardiac surgery. Consistent with reports in ACS patients,(1) we found a differential impact of hyperglycemia on PMI in patients with and without previously recognized diabetes (worse in non-diabetics). The interaction between insulin requirements and intraoperative hyperglycemia suggests a detrimental effect of insulin resistance in PMI severity. Our results indicate that the critical window of myocardial vulnerability from hyperglycemia in cardiac surgical patients may begin in the operating room. Establishing adequate metrics of intraoperative glycemic control and targets in diabetic and non-diabetic patients form the object of future investigations.

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## INTRAOPERATIVE MAGNESIUM ADMINISTRATION DOES NOT DECREASE NEUROCOGNITIVE DYSFUNCTION AFTER CARDIAC SURGERY

Mathew J; Lombard F; Mackensen G; White W; Blumenthal J; Newman M

*Duke University Medical Center*

**Introduction:** Neurocognitive decline occurs frequently in the elderly after cardiac surgery, and persists in an important percentage of patients. Magnesium (Mg) may provide neuroprotection through preservation of cellular energy metabolism, blockade of the NMDA receptor, diminution of the inflammatory response, and inhibition of platelet activation. We therefore hypothesized that intraoperative magnesium administration would decrease postoperative cognitive impairment.

**Methods:** After IRB approval, 389 patients  $\geq 55$  years in age undergoing CABG [SPCHAR(plusmn)] valve surgery were enrolled into this prospective, randomized, double-blind, placebo-controlled trial. Patients were excluded if they had a history of symptomatic cerebrovascular disease, uncontrolled hypertension, creatinine  $>2$  mg/dL,  $<7$ th grade education, or had a Mini Mental State Examination score  $<24$ . Patients were randomized to receive either placebo or Mg immediately after induction of anesthesia as a 50 mg/kg bolus over 20 minutes followed by another 50 mg/kg infusion over 3 hours (total dose 100 mg/kg). Patients were also evaluated with a well-validated battery of 5 cognitive tests on the day before surgery and again at 6 weeks. Cognitive deficit was defined by factor analysis as a decline of one standard deviation or more in at least 1 of 4 cognitive domains. A change score was also calculated by subtracting the baseline from the follow-up mean of the 4 domain scores. The effect of magnesium on postoperative cognition was tested using multivariate modeling accounting for age, years of education, and baseline cognition;  $p < 0.05$  was considered significant.

**Results:** 196 patients were randomized to receive Mg and 193 to placebo. 305 of these subjects underwent CABG surgery, 60 had valve surgery, and 24 had CABG + valve surgery. As expected from randomization, there were no differences between the Mg and placebo groups with respect to age, gender, years of education, baseline cognition, weight, history of diabetes, and bypass and cross-clamp times. Serum Mg levels were significantly higher in the Mg treatment group (Figure). Cognitive deficits at 6 weeks after surgery were present in 44.9% of subjects randomized to Mg and in 44.3% of subjects randomized to placebo ( $p = 0.91$ ). The continuous cognitive score was also not significantly different between the treatment groups (Mg: 0.07 [SPCHAR(plusmn)] 0.29 vs. placebo: 0.12 [SPCHAR(plusmn)] 0.28;  $p = 0.10$ ). Multivariate modeling revealed no effect of Mg when either the cognitive deficit ( $p = 0.81$ ) or continuous change score ( $p = 0.15$ ) was examined. In a subset of patients with baseline Mg  $< 1.6$  mg/dl, Mg treatment was protective. Adverse events including bleeding, stroke, and death were not different between treatment groups.

**Conclusions:** Despite significantly higher Mg levels in the intraoperative and immediate postoperative period, intraoperative Mg therapy did not decrease neurocognitive dysfunction after cardiac surgery.

## INTRAOPERATIVE SYSTOLIC BLOOD PRESSURE AND SHORT TERM POSTOPERATIVE RENAL FUNCTION

Wood M; Aronson S; Phillips-Bute B

*Duke University*

**Introduction:** Intraoperative blood pressure management although common during cardiac surgery is guided by few data. Recent evidence suggests an association between intraoperative systolic blood pressure (SBP) variability and 30 day mortality (1,2). We sought to explore an association between intraoperative SBP variability and postoperative renal function outcomes in patients undergoing cardiac surgery.

**Methods:** After IRB approval, we examined data on 4865 patients undergoing coronary artery bypass grafting (CABG) surgery at Duke University from the Duke Heart Center database between 09/01/1996 and 12/31/2005. Electronically captured blood pressure recordings (Q30sec) from arterial line measurements were collected in all patients. Pressure measurements during cardiopulmonary bypass were excluded from analysis. SBP variability was evaluated by the integrated summation of cumulative blood pressure incursions above and below threshold [Area Under Curve (AUC) defined as magnitude in mmHg times duration in minutes], AUC for 20% above and below baseline blood pressure was calculated. Baseline SBP was defined as the mean SBP over the first 5 recordings after arterial line placement. In addition, the number of incursions above or below threshold, the mean magnitude (mmHg) per incursion above or below threshold, the cumulative minutes above or below threshold, and the cumulative minutes per incursion above or below threshold. Multiple logistic regression was used to evaluate % change creatinine (baseline before surgery to max postoperative Cr value up to POD 10) adjusting for preoperative risk factors (including pulse pressure) for postoperative renal injury.

**Results:** 4184 (86%) patients underwent CABG with CPB, 389 (8%) patients underwent off bypass CABG (OPCAB), 292 (6%) patients underwent combined CABG/valve surgery. SBP variability was evaluated in 4098 patients with 767 patients not evaluated due to missing covariate information. Mean SBP incursion <95mmHg was significantly associated with a % change creatinine ( $p < 0.01$ ). In addition, AUC for 20% below baseline and AUC for 20% both above and below baseline appear to predict postoperative renal dysfunction depending on preoperative pulse pressure.

**Conclusion:** The Intraoperative SBP variability index of mean incursion nadir < 95mmHg is associated with worse postoperative renal function defined by %change creatinine. In addition, those patients with greater SBP variability from their baseline as defined by AUC for 20% of baseline suggest an association with worse postoperative renal function.

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## IS ETOMIDATE ASSOCIATED WITH ADVERSE OUTCOMES FOLLOWING CARDIAC SURGERY?

Anthony D; Wagner C; Duncan A; Xu M

*The Cleveland Clinic*

### Introduction

Etomidate is an intravenous anesthetic agent used for induction of anesthesia and for procedural sedation in the intensive care unit. Etomidate causes suppression of adrenal glucocorticoid and mineralocorticoid production. In fact, adrenal suppression has been observed even after a single dose of etomidate. Because of etomidate-induced adrenal suppression, administration of etomidate has been associated with an increased incidence of adverse events in critically ill patients in septic shock. However, the clinical impact of etomidate use on outcomes following cardiac surgery has not been examined. The purpose of our study is to determine whether use of etomidate as compared to sodium thiopental for induction of anesthesia may negatively impact postoperative in-hospital outcomes in cardiac surgical patients.

### Methods

The Cleveland Clinic Department of Cardiothoracic Anesthesia Registry was used to identify patients who were administered etomidate or sodium thiopental for induction of anesthesia during coronary artery bypass grafting and/or valve surgery from October 1, 2005 to May 31, 2007. Patients receiving 20 to 40 mg of etomidate were included in the analysis. Univariate analysis was performed to assess the association between predictor variables and in-hospital cardiac morbidity and mortality. Cardiac morbidity was defined as the combination of either post-operative myocardial infarction and/or low cardiac output with a requirement for intra-aortic balloon pump, ventricular assist device, or extracorporeal membrane oxygenation. Associated single variables were placed into a multivariable model, and, logistic regression with backward selection was used to evaluate the effect of etomidate compared to sodium thiopental on morbidity and mortality.

### Results

A total of 1,765 patients received etomidate and 1,422 patients received sodium thiopental during the study period and satisfied inclusion criteria. For patients receiving etomidate, 17 (0.96%) patients experienced cardiac morbidity and 29 (1.6%) patients died. In the patients receiving sodium thiopental, 20 (1.4%) patients experienced cardiac morbidity and 38 (2.7%) patients died. Risk-adjusted analysis found no increase in cardiac morbidity [OR (95% CI) of 0.69 (0.35, 1.38)] or mortality [0.60 (0.36, 1.07)] associated with etomidate use.

### Conclusions

These results suggest that use of etomidate for anesthetic induction is not associated with an increased incidence of mortality or cardiac morbidity following cardiac surgery compared to sodium thiopental.

# IS THE STROKE VOLUME VARIATION A GOOD PREDICTOR OF HEMODYNAMIC INSTABILITY AT THE AORTIC UNCLAMPING DURING ABDOMINAL AORTIC ANEURYSM REPAIR SURGERY?

ONUKE E; SEINO Y; TOMITA Y; KUROKAWA S; NOMURA M; DOI K; OZAKI M

*Tokyo Women's Medical University*

## [Background]

Hemodynamic changes from aortic unclamping during abdominal aortic aneurysm (AAA) repair are influenced by several factors such as the length of aortic cross clamping time, the site of clamping and especially intravascular volume status. Accordingly, fluid optimization before aortic unclamping is important to avoid hemodynamic instability. Stroke volume variation (SVV) is a good indicator of fluid responsiveness, but the effectiveness of optimizing SVV during AAA repair has not been confirmed. To this point, we investigated whether low blood pressure after unclamping could be predicted with SVV.

## [Methods]

Thirty-one consecutive patients underwent abdominal aortic reconstruction surgery were enrolled in this study. The FloTrac™ system (Edwards Lifesciences LLC, Irvine, CA) and PreSep™ central venous oximetry catheter (Edwards Lifesciences LLC, Irvine, CA) were used, and systolic arterial pressure, SVV, central venous pressure (CVP) and superior vena caval oxygen saturation (ScvO<sub>2</sub>) were monitored. Four patients received anesthesia intravenously with propofol while the other 27 patients were anesthetized using sevoflurane. Systolic arterial pressure, SVV, CVP and ScvO<sub>2</sub> at the 3 minutes prior to and after aortic unclamping were analyzed. Statistical analysis was conducted using the paired t-test and Spearman's rank-correlation coefficient method. A p<0.05 was considered statistically significant. All figures are displayed as the average ± the standard deviation.

## [Results]

The mean age of the patients was 67.3 ± 11.3 years and 25 patients (80.6%) were male. Primary diseases were abdominal aortic aneurysm (24 cases), common iliac artery aneurysm (4 cases), internal iliac artery aneurysms (1 case), arteriosclerosis obliterans (1 case) and aortic aneurysm dissection (1 case). Before and after unclamping, systolic arterial pressure and ScvO<sub>2</sub> decreased significantly from 107.3 ± 17.4 to 91.4 ± 13.6 mmHg and 84.3 ± 7.3% to 82.8 ± 8.3% respectively. SVV had no significant change (15.0 ± 9.0 vs. 15.7 ± 8.5%). No correlations were found between SVV and systolic arterial pressure changes nor CVP and systolic pressure changes before and after unclamping. SVV and ScvO<sub>2</sub> changes also showed no correlation before and after unclamping.

## [Discussion and Conclusions]

SVV failed to predict hemodynamic instability derived from aortic unclamping during AAA repair surgery. The reason seems to be that arterial pulse pressure waveform changes with massive afterload increase just like aortic stenosis or regurgitation.

ScvO<sub>2</sub> decreased significantly after unclamping in parallel with decrease in systolic arterial pressure and it suggests that ScvO<sub>2</sub> can show the result of hemodynamic imbalance due to sudden cardiac output decrease.

In this clinical setting, it is important to combine multiple parameters to assess the fluid management, and further investigation is required to use SVV as a preload marker.

## LUNG TRANSPLANTATION IN PATIENTS WITH CORONARY ARTERY DISEASE

SUBRAMANIAM K; MARQUEZ J; SULLIVAN E; TOYODA Y

*UPMC*

**Purpose:** Patients with advanced age are being listed for lung transplantation (LTX). Many of these patients have coronary artery disease (CAD) detected by cardiac catheterization. Perioperative morbidity and mortality of these patients undergoing LTX is unknown. Therefore, we evaluated the outcomes of these patients in this retrospective study.

**Methods:** After approval from institutional review board, we reviewed records of patients who underwent LTX between September 2007 and May 2008.

**Demographics, preoperative cardiac tests, intraoperative parameters** (cardiopulmonary bypass, ischemic time, inotropic requirement, ischemic episodes and arrhythmias) and postoperative major organ dysfunction (respiratory, renal, cerebral and cardiac) and mortality were recorded. CAD patient's data was compared with non-CAD patients who underwent LTX during the same period.

**Results:** Sixty six patients received LTX, of whom 31 patients had CAD. Two had previous bypass surgery (CABG) with patent grafts, two others had concomitant CABG and LTX and 13 patients had cardiac stents. Rest of the patients underwent LTX without any cardiac intervention. Mean age of the patients were higher (65 years versus 46 years,  $P < 0.001$ ) and there were more men than women in CAD group ( $P = 0.04$ ). Mean pulmonary artery pressures and transpulmonary gradients were higher in non-CAD group. Mean ejection fraction and number of patients with diastolic dysfunction were similar. History of smoking was higher in CAD group (28% in non-CAD vs 93% in CAD group,  $P < 0.001$ ). Anemia, ethanol use, hypertension, arrhythmias, diabetes, renal and cerebrovascular disease were comparable. More CAD group patients were treated with aspirin and statins. CAD group had more patients with COPD and non-CAD group had more patients with cystic fibrosis. 88% in non-CAD group and 72% in CAD group had double LTX ( $P = 0.17$ ). Requirement for cardiopulmonary bypass was higher ( $P = 0.04$ ) in non-CAD group (51%) than CAD group (26%). Wall motion changes, arrhythmias, requirements for inotropes, vasopressors and nitric oxide were comparable. Respiratory, cardiac and renal failure, stroke, sepsis, length of hospital stay and overall mortality (11% in non-CAD group vs 9.7% in CAD group,  $P = 0.59$ ) were similar. Atrial fibrillation developed more significantly ( $P = 0.009$ ) in CAD (36%) group compared to non-CAD (8.5%) group.

**Conclusion;** Patients with CAD undergoing lung transplants have comparable morbidity and mortality to non-CAD patients. Atrial fibrillation occurred more commonly in patients with CAD.

## METABOLOMIC PROFILING OF PLASMA FROM INDIVIDUALS UNDERGOING CARDIAC SURGERY WITH PLANNED MYOCARDIAL ISCHEMIA-REPERFUSION REVEALS EARLY MARKERS OF PERIOPERATIVE MYOCARDIAL INJURY

Lobato R; Turer A; Mathew J; Newgard C; Podgoreanu M

*Duke University*

**Background:** Cardioplegic arrest is used routinely during cardiac surgery, yet this form of ischemia-reperfusion (I/R) injury is relatively poorly characterized in terms of its myocardial metabolic consequences. We performed targeted metabolomic analysis to establish a metabolic signature of perioperative myocardial injury (PMI).

**Methods:** With IRB approval, 37 patients undergoing elective cardiac surgery with CPB were enrolled at a single institution. Matched arterial and coronary sinus plasma samples collected before and 10 minutes following aortic cross-clamp placement were analyzed for myocardial fuel substrates, 15 aminoacids, and 43 acylcarnitines using mass spectrometry. Transcoronary extraction ratios (ER) were calculated for each metabolite. PMI severity was assessed using postoperative day 1 plasma levels of CK-MB (Siemens, ULN 5ng/ml). Nonparametric statistics were used to test differences between substrate ER by baseline comorbidities and correlation with postoperative outcomes. Principal Component Analysis (PCA) was performed on post-I/R ER and used in multiple regression models of PMI.

**Results:** We identified robust changes in transmyocardial ER from before to after I/R (Fig 1a). CAD patients displayed significant differences in baseline myocardial ER of a number of substrates (lower FFA, 3-HB, and GLX uptake and greater ALA elution). Following I/R, significantly lower ER of glucose, total ketones, 3-HB, lactate, and GLX and greater release of ALA were especially evident in patients with pre-existing LV dysfunction. After I/R, there was significant release of two acyl-carnitine species (acetyl-carnitine and 3-hydroxybutyryl-carnitine). PCA of the post-I/R metabolic extraction ratios revealed two principal components that were independently associated with PMI severity (Fig 1b). Furthermore, PC1 scores were significantly correlated with pre-operative fractional area change ( $r=0.37$ ,  $p<0.04$ ), total dose of epinephrine used in the first 60 minutes following wean from CPB ( $r=-0.42$ ,  $p<0.02$ ) and longer durations of postoperative inotropic support ( $r=-0.30$ ,  $p=0.09$ ). PC2 scores were associated with higher cardiac outputs off-CPB ( $r=0.39$ ,  $p=0.06$ ) and over the first 4 hours in the ICU ( $r=0.52$ ,  $p=0.007$ ). PC3 scores directly correlated with higher doses of epinephrine in the 60 minutes following CPB ( $r=0.39$ ,  $p<0.03$ ).

**Conclusions:** Our results identify a potential role for intraoperative metabolic profiling in the early detection of PMI and conduct of cardioprotective strategies. The pre-existing ventricular state is associated with significant differences in metabolic profiles at baseline and following I/R, with the dysfunctional ventricle particularly susceptible to these insults. Furthermore, beyond impairment in substrate extraction, the myocardium demonstrates a defect in oxidative metabolism of the substrates it does uptake following I/R.

## MODIFIED THROMBOELASTOGRAPHY HAS THE POTENTIAL TO INVESTIGATE SPECIFIC PLATELET RECEPTOR DYSFUNCTION ASSOCIATED WITH CARDIOPULMONARY BYPASS

Weitzel N; Seres T

*University of Colorado Health Sciences Center*

### Introduction:

Platelet dysfunction is a known side effect of cardiopulmonary bypass (CPB)(1). Platelet Mapping™, a modification of Thromboelastography (TEG®), assesses platelet function by comparing the function of arachidonic acid (AA) and adenosine-5-diphosphate (ADP) receptors to thrombin receptors(2). This technique was applied in our study to investigate the effect of CPB on platelet receptor function. Furthermore, a novel assay was developed to examine the function of collagen receptors before and after CPB.

### Methods:

Following IRB approval, 26 patients have been enrolled in this study until now. Blood samples were collected before and after CPB. The MA parameter of the TEG represented the function of thrombin receptors (MATEG). Heparinized blood samples were combined with either reptilase/Factor XIIIa alone, measuring the fibrin contribution (MAfibrin), or with AA, ADP or Collagen evaluating each receptor (MAAA, MAADP, MACollagen) as percent activation of thrombin. An example for AA receptor activation:

Percent ActivationAA(%)=(MAAA –MAfibrin) - / (MATEG – MAfibrin) x 100 (2).

Data collected included: demographics, CPB time, cross clamp time, percent activation, and post-operative blood loss in 24 hours. Patients were divided into high bleeding group (blood loss ≥ 850 ml/24 hours) and low bleeding group (blood loss < 850 ml/24 hours).

### Results:

There were no significant differences between demographic data of bleeding groups (Table 1). The percent activation of each receptor decreased after CPB in both groups. There were no significant differences in post bypass function of thrombin, AA, and ADP receptors between bleeding groups. At the same time the post bypass function of collagen receptor decreased significantly in the high bleeding group (Table 2).

### Conclusions:

This pilot study was designed to determine the contribution of platelet receptor function in clinically significant bleeding following CPB. When comparing the bleeding groups, we were able to show a significant difference only between collagen receptor activities, suggesting that this receptor may play a key role in platelet function for clot formation following CPB. Further studies into the platelet collagen receptor may allow for better prediction of postoperative bleeding and potential pharmacologic therapy.

### References:

1. Paparella D, Brister SJ, Buchanan MR. Coagulation disorders of cardiopulmonary bypass: a review. *Intensive Care Medicine* 2004;30:1873-81.
2. Haemoscope. Guide to Platelet Mapping™. Haemoscope Corporation 2004-2006.

## N-ACETYLCYSTEINE FOR THE PREVENTION OF ACUTE RENAL FAILURE AFTER CARDIAC SURGERY: A META-ANALYSIS OF RANDOMIZED TRIALS

Wang G; Bainbridge D; Martin J; Cheng D

*Fuwai hospital and Cardiovascular institute; London Health Science Center, University of Western Ontario; London Health Sciences Centre, University of Western Ontario; London Health Sciences Centre, University of Western Ontario,*

**Background:** Acute renal failure (ARF) is associated with an increase in morbidity, mortality for cardiac surgical patients. N-acetylcysteine (NAC) reduces proinflammatory cytokines, oxygen free-radical production, and ameliorates ischemia reperfusion injury during cardiac surgery, and therefore may theoretically attenuate renal injury. The aim of this study was to determine, through systematic review and meta-analysis of all relevant randomized trials, whether NAC prevented the development of ARF in patients undergoing cardiac surgery. In addition, the effect of NAC on mortality, morbidity and resource utilization was examined.

**Methods:** A comprehensive search was undertaken to identify all randomized trials of NAC used in cardiac surgery. MEDLINE, Cochrane Library, EMBASE, and abstract databases were searched up to October 2008. All randomized trials comparing the use of NAC versus placebo during cardiac surgery, in any language and reporting at least one predefined outcome were included. The random effect model of comprehensive meta-analysis version 2.2 was used for analysis of all outcomes. Odds ratios (OR, 95% confidence intervals [CI]) and weighted mean differences (WMD, 95% CI) were calculated for dichotomous and continuous variables, respectively.

**Results:** A total of 15 randomized trials involving 1407 patients were included. During cardiac surgery, the use of NAC was not associated with a decrease in acute renal failure (OR 0.86, 95% CI 0.66-1.12,  $p=0.26$ ), acute renal failure requiring dialysis (OR 1.05, 95% CI 0.52-2.11,  $p=0.90$ ), or mortality (OR 0.80, 95% CI 0.38-1.69,  $p=0.56$ ). There were also no difference of the incidence of atrial fibrillation (OR 0.67, 95% CI 0.37-1.22,  $p=0.19$ ), acute myocardial infarction (OR 0.69, 95% CI 0.29-1.61,  $p=0.39$ ), intra-aortic balloon pump support (OR 0.64, 95% CI 0.31-1.32,  $p=0.23$ ), stroke (OR 0.78, 95% CI 0.30-2.03,  $p=0.61$ ) or re-exploration for bleeding (OR 0.91, 95% CI 0.44-1.90,  $p=0.80$ ) between NAC and placebo.

The use of NAC had no impact on length of ventilation (WMD -0.43 hours, 95% CI -1.51 to 0.65,  $p=0.43$ ), ICU stay (WMD 0.03 days, 95% CI -0.04 to 0.10,  $p=0.38$ ), and hospital LOS (WMD 0.40, 95% CI -0.94 to 1.74,  $p=0.56$ ).

**Conclusion:** Current evidence shows that the perioperative use of NAC did not prevent ARF and also had no effect on the other clinical outcomes in patients undergoing cardiac surgery.

## NF-KB INHIBITORY PEPTIDE AND PPAR-ALPHA AGONIST ATTENUATE HYPERGLYCEMIC EXACERBATION OF MYOCARDIAL ISCHEMIA/REPERFUSION INJURY IN A RAT MODEL OF CARDIOPLEGIC ARREST

Zhang Z; Ma Q; Mackensen G; Podgoreanu M

*Duke University Medical Center*

**Background:** Ischemia-reperfusion (I/R) and inflammation modulate severity of myocardial injury associated with cardiac surgery. While acute hyperglycemia was reported as an independent predictor of cardiovascular morbidity and mortality, its role and mechanisms in exacerbating perioperative myocardial I/R injury remain unclear. We tested the hypothesis that the acute hyperglycemic exacerbation of perioperative myocardial I/R injury can be attenuated by modulation of NFkB and peroxisome proliferator-activated receptor alpha (PPAR-alpha) pathways in a novel rodent model of acute hyperglycemia and cardioplegic arrest(CA).

**Methods:** With IACUC approval, 15 male Sprague-Dawley rats were randomly assigned to 5 groups: cardioplegic arrest (CA), cardiac arrest+hyperglycemia (CAHG), NF-kB inhibitory peptide (NIP), PPAR-alpha agonist, Wy14643 (PA), and combination therapy (NIP+PA). All animals underwent 75 min of moderate hypothermic CPB with 45 min of CA using blood cardioplegia. Acute hyperglycemia was induced in all experimental groups except CA using 25% Dextrose (5gm/kg) administered preoperatively 0.75gm intraperitoneally (ip), intraoperatively 0.25gm in CPB prime and 0.5gm/hr intravenously (iv), and postoperatively 0.5gm ip, with perioperative glucose levels maintained >300 mg/dl. Animals from treatment groups received either NF-kB inhibitory peptide (1mg/kg), PPAR-alpha agonist (1mg/kg) or their combination before (ip), during (with cardioplegia), and after CPB (ip), whereas CA animals received saline. No animals received insulin. At 24 h after CPB animals were sacrificed and hearts harvested for analysis. Myocardial apoptosis was quantified using both activated caspase-3 (Western blot) and TUNEL assays. Myocardial necrosis was quantified as plasma levels of cardiac troponin I (cTnI) and heart-type fatty acid binding protein (hFABP) using ELISA.

**Results:** Hyperglycemia exacerbated myocardial I/R injury, as evidenced by significantly increased cTnI (4.7 +/- 0.2 vs. 1.6 +/- 0.2,  $P < 0.0001$  vs. CA), hFABP (87.7 +/- 15.0 vs. 7.8 +/- 3.4,  $P < 0.005$  vs. CA), and caspase-3 activity. Both the NF-kB inhibitor, Wy14643, or their combination attenuated perioperative myocardial I/R injury, as confirmed by significantly decreased cTnI (2.1 +/- 0.5, 1.5 +/- 0.3 and 1.4 +/- 0.1 vs. 4.7 +/- 0.2, respectively,  $P < 0.01$  vs. CAHG), hFABP (12.4 +/- 2.6, 2.7 +/- 0.7 and 6.5 +/- 4.1 vs. 87.7 +/- 15.0, respectively,  $P < 0.01$  vs. CAHG) (Fig. 1 a, b), caspase-3 activity, and number of apoptotic myocardial cells (Fig. 1c).

**Conclusions:** We provide preclinical evidence for acute hyperglycemic exacerbation of myocardial injury in a clinically relevant rodent model of cardioplegic arrest, by employing robust metrics of perioperative myocardial necrosis and apoptosis. Preliminary mechanistic analysis suggests the involvement of the PPARalpha-NF-kB axis, as evidenced by the significant attenuation of injury in animals receiving NFkB inhibitory peptide or PPAR-alpha agonist.

## PATTERN OF MYOCARDIAL DYSFUNCTION AFTER CROSS CLAMP APPLICATION (TEE EVIDENCE FOR ANREP EFFECT)

Zhao X; Matyal R; Subramaniam B; Mahmood F; Mitchell J; Bhakta A; Hess P

### *Department of Anesthesiology*

**Background:** Aortic cross clamp (XCL) application during abdominal aortic aneurysm (AAA) surgery is associated with changes in myocardial systolic and diastolic function. Sudden increases in after-load have also shown to transiently increase the myocardial contractility (Anrep Effect). We assessed myocardial function with transesophageal echo (TEE) after XCL application to observe changes in myocardial function.

**Methods:** After IRB approval, 20 patients undergoing elective AAA surgery were consented to participate in the study. TEE examinations were carried out after induction of general anesthesia. We utilized myocardial performance index (MPI), an index of global myocardial performance, to assess serial changes in myocardial function. A baseline MPI was calculated by using pulse wave Doppler (PWD) by the described methodology:  
Isovolumetric Contraction Time + Isovolumetric Relaxation Time  
Ejection Time

An MPI value of  $>0.35$  was considered abnormal. Further assessments of MPI were made 2 minutes, 10 minutes and 20 minutes after XCL application. The final MPI was calculated 10 minutes after aorta was unclamped (Figure 1).

**Results:** A total of 20 patients completed the study. There were 6 females and 14 males. Average age was 67.2 years (47-83 years). The MPI values were 0.28 ( $\pm$  0.13) at base-line, 0.40 ( $\pm$  0.18) after two minutes, 0.31 ( $\pm$  0.17) after ten minutes, 0.36 ( $\pm$  0.16) twenty minutes after XCL application and was 0.18 ( $\pm$  0.11) ten minutes after un-clamping of aorta (Fig 1). The change in MPI from baseline to two minutes post-XCL was significant ( $p= 0.007$ ), not significant at ten minutes and twenty minutes post-XCL ( $p= 0.45$  &  $0.12$  respectively).

**Discussion:** Our study demonstrates that the myocardial function worsens (Prolonged MPI) two minutes after XCL application. The myocardial function then returns to baseline 10 minutes after XCL application. Our results are consistent with earlier reports of "transient improvement" in myocardial function (2-10 minutes) after sudden increases in after-load, "Anrep Effect".

## PERIOPERATIVE ANTITHROMBIN ACTIVITY IS POORLY ASSOCIATED WITH MAJOR ADVERSE CARDIAC EVENTS AFTER CORONARY ARTERY BYPASS GRAFTING

Garvin S; Collard C; Chen J; Muehlschlegel J; Perry T; Liu K; Fox A; Aranki S; Shernan S; Body S

*Baylor College of Medicine, Saint Luke's Episcopal Hospital; Brigham and Women's Hospital; Talecris Biotherapeutics*

### Background:

Acquired antithrombin (AT) deficiency is common in patients with critical illness, hepatic dysfunction and after cardiac or other major surgery (1). Low levels of AT have been associated with prolonged ICU stay and a higher incidence of neurologic and thromboembolic events after cardiac surgery (2). We hypothesized that perioperative AT activity is independently associated with postoperative major adverse cardiac events (MACE) in patients undergoing coronary artery bypass graft (CABG) surgery.

### Methods:

The study cohort (n = 1403) was a prospective study of patients undergoing primary CABG surgery with cardiopulmonary bypass (CPB) between August 2001 and May 2006 (<http://clinicaltrials.gov/show/NCT00281164>). Detailed perioperative data was recorded. The primary clinical end point was occurrence of MACE, defined as a composite outcome of any one or more of: operative death, reoperation for coronary graft occlusion, myocardial infarction, stroke, pulmonary embolism, or cardiac arrest until first hospital discharge. Plasma AT activity was measured using a colorimetric method (Siemens Healthcare Diagnostics, Tarrytown, NY) prior to induction of general anesthesia, five minutes after post-CPB protamine, and on postoperative days (POD) 1-5. Multivariate logistic regression modeling was performed to estimate the independent effect of perioperative AT activity on MACE.

### Results:

Patient demographics and perioperative risk factors are described in Table 1. MACE occurred in 146 patients (10.4%), consisting of postoperative mortality (N=12), MI (N=108), stroke (N=17), pulmonary embolism (N=8), cardiac arrest (N=16) or treatment for graft occlusion (N=6). AT activity at baseline did not differ between patients with ( $0.91 \pm 0.13$  IU/mL; n=146) and without ( $0.92 \pm 0.13$  IU/mL; n=1257) (P=0.18) MACE. Similarly, postoperative AT levels did not significantly differ in patients with and without MACE, with AT activity in both groups being significantly reduced immediately post-CPB and recovering over the ensuing 5 postoperative days to baseline. MACE was associated with AT activity, but only on POD 2 and beyond (Table 2).

### Conclusions:

Preoperative AT activity is not associated with MACE after CABG surgery. MACE is associated with postoperative AT activity, but only at time points occurring predominantly after the MACE event.

### References:

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2. Ranucci M, et al. Postoperative antithrombin levels and outcome in cardiac operations. *Crit Care Med* 2005;33:355-60.

## PERIOPERATIVE STATIN THERAPY DECREASES THE RISK OF ATRIAL FIBRILLATION AFTER CARDIAC SURGERY

Mathew J; Collard C; Fontes M; Miao Y; Mangano D

*Duke University Medical Center; Ischemia Research and Education Foundation; Texas Heart Institute; Weill Medical College of Cornell University*

**Introduction:** Atrial fibrillation (AF) is a common, but potentially preventable, complication of cardiac surgery with a global incidence ranging between 27-40%. Recent data have suggested that preoperative treatment with hydroxymethyl-glutaryl-coenzymeA reductase inhibitors (statins) is associated with a reduction in the incidence of postoperative AF. Therefore, utilizing data from a large observational study, we sought to determine if preoperative and/or postoperative statin therapy decreases the occurrence of new-onset postoperative AF and if statin therapy alters the previously established multicenter risk index for AF.[SPCHAR(sup1)]

**Methods:** The McSPI EPI II observational study was prospective, enrolling 5436 cardiac surgical patients from 72 centers among 17 countries, following IRB approval. Using a derivation cohort (n=3093 patients), associations between predictor variables, including statin therapy, and postoperative AF were determined with bivariate analysis, and models were derived in a sequential fashion using multivariable logistic regression. The final model was assessed using a validation cohort (n=1564 patients) and a risk index for AF was developed. Model entry and retention criteria were set at  $P < 0.2$  and  $P < 0.01$ , respectively.

**Results:** Of the 4657 CABG or CABG [SPCHAR(plusmn)] valve patients included in this study, 1503 patients (32.3%) developed postoperative AF. Preoperative and postoperative treatment with statins resulted in a 13% absolute risk reduction in AF and a 42% reduction in the odds for AF ( $p < 0.001$ ; Table 1). Other risk factors associated with AF were advanced age, history of AF or chronic obstructive pulmonary disease, valve surgery, and withdrawal from ACE inhibitor or beta-blocker therapy. Conversely, reduced risk was associated with administration of beta-blockers, ACE inhibitors, potassium and NSAIDs (Table 1). The area under the ROC curve when applying the final risk model to the validation cohort was 0.77. A risk score  $< 7$  was associated with 11.7% chance of developing AF (low risk); 7-24 with 30.3% (medium risk); and  $> 24$  with 66.9% chance (high risk).

**Conclusions:** The combination of preoperative and postoperative statins further reduces the risk of new-onset AF after cardiac surgery.

### Reference:

1. Mathew JP, et al. JAMA 2004; 291:1720-9.

## POST APROTININ ERA: IS E-AMINOCAPROIC ACID AS GOOD IN COMPLEX AORTIC SURGERY?

Fontes M; Girardi L; Koval K; Feiler D; Ahn H; Karkera M; Latmore M; Skubas N

*Weill Medical College of Cornell University*

**Introduction:** Replacement of the ascending aorta/arch due to dissection or aneurysm is associated with major bleeding requiring use of a variety of therapies including transfusion of blood products and administration of several hemostatic pharmacological agents. However, nearly one year ago, controversy about the safety of aprotinin – a serine protease inhibitor used primarily in such complex procedures, resulted in termination of its use in North America. It is our hypothesis that the incidence of major bleeding and transfusion practice is the same during the period immediately before and after discontinuation of aprotinin.

**Methods:** With Institutional Review Board Approval, we conducted a study on a cohort of patients who underwent surgery for replacement of the ascending aorta/arch from March 2007-July 2008. From this population, we identified a group who received aprotinin [APRO; Excel Random Selection] and a group that received Epsilon Aminocaproic Acid (EACA; 11/2007-7/2008). Data on demographics, preoperative, physiologic, laboratory, surgical, and cardiopulmonary bypass (CPB) characteristics were collected. Outcomes of interest included 24-hour transfusion requirements of red blood cells (RBC), fresh-frozen plasma (FFP), Platelets (PLT), and cryoprecipitate; 24-hour chest tube output; renal outcomes and incidence of “chest exploration” for bleeding. All patients underwent hypothermic non-pulsatile CPB using standard techniques and maintaining mean arterial pressure (MAP) between 60-80 mm Hg. Kaolin was used in APRO and celite for EACA ACT measures. For patients requiring circulatory arrest (CA), systemic hypothermia to a bladder temperature of  $<20\text{ }^{\circ}\text{C}$  (tympanic temperature also monitored) and retrograde cerebral perfusion at a flow of approximately 150 ml/min (to achieve a perfusion pressure  $<25$  mm Hg) were instituted. Analysis included Student’s t-test, Fisher’s exact test, and Chi square where applicable and results are presented as mean + SD and %. P of  $< 0.05$  was considered significant.

**Results:** In all, 106 patients were studied, with half in each group. Table 1 shows the demographic and surgical characteristics of the APRO and the EACA groups, which were similar with exception of history of COPD (EACA) and preoperative hematocrit and total dose of intraoperative heparin (APRO). No difference was observed between the groups in relation to 24-hour transfusion requirement or chest tube output, renal outcomes, and hospital length of stay (Table 2).

**Conclusion:** In this preliminary study, we were not able to demonstrate a superior hemostatic effect of aprotinin use in major aortic surgery over EACA.

## POSTOPERATIVE PULMONARY DYSFUNCTION AFTER CABG SURGERY: A PREDICTIVE MODEL

Cuthbert Hudson J; Stafford Smith M; Phillips-Bute B; Hudson C; Young C; Gaca J; Welsby I; Bartz R

*Duke University; VAMC*

### Intro:

Postoperative pulmonary dysfunction is highly associated with mortality after aortocoronary (CABG) surgery.<sup>(1)</sup> Attempts to reduce postoperative pulmonary morbidity have met with limited success, and although individual risk factors have been identified, no predictive model exists to identify high-risk patients and target them for optimization. Therefore, we tested the hypothesis that a model can be developed to predict patients' risk for pulmonary dysfunction after CABG surgery.

### Methods:

With IRB approval, consecutive nonemergent CABG surgery patients between Sep93 to Jun01 were included for analysis in this retrospective observational study. Patients undergoing off-pump or valvular surgery, or who were in shock preoperatively were excluded. Pulmonary dysfunction was defined as postoperative pulmonary edema, pneumonia, and/or ARDS. From a list of possible predictors of postoperative pulmonary complications, (age, gender, cross-clamp time, blood products, respiratory and other comorbidities) variables with  $p < 0.1$  significance on univariate logistic regression were selected for inclusion in a multivariable model. Non-significant predictors were dropped from the model until only significant variables remained.

### Results:

Demographics were similar to those seen in other studies.<sup>(1)</sup> Of the 3627 patients 281 had missing data and were excluded. Overall, 293 patients (8.76%) developed postoperative pulmonary dysfunction. Multivariable logistic regression analysis identified pump time, RBC transfusion within 48h, baseline creatinine, obesity, and redo surgery as significant independent predictors; odds ratios were 1.005 ( $p < 0.0001$ ), 1.081 ( $p = 0.005$ ), 1.18 ( $p < 0.0001$ ), 1.527 ( $p = 0.02$ ), and 1.809 ( $p = 0.03$ ), respectively.

### Conclusion:

We developed a predictive model for postoperative pulmonary dysfunction after CABG surgery that includes patient factors (preoperative creatinine and obesity) and procedural factors (pump time, number of RBCs transfused, and redo surgery). Unexpectedly, some risk factors were not independently predictive (eg. COPD, smoking history), however additional studies will be necessary to validate this model. Prediction of pulmonary dysfunction may be useful as a tool for preoperative risk stratification but also for identifying high-risk patients for evaluation of potential protective strategies.

### Reference:

1) Milot J. et al, Chest 2001; 119: 884-888

## PRACTICAL ANATOMIC LANDMARKS FOR DETERMINING THE INSERTION DEPTH OF CENTRAL VENOUS CATHETER IN PAEDIATRIC PATIENTS

Kim J; Kim C; Kim S; Na H

*bun-dang seoul national university hospital; Seoul National University Hospital; SNUH*

**Background:** Various methods have been recommended to decide a proper insertion depth of central venous catheter (CVC). When we decide the depth of CVC just based on the patient's characteristics such as height or age, it does not make up for various puncture sites. The puncture site at the lower part of the neck can lead to a dangerous deep insertion of CVC while the insertion at the upper part produces too shallow insertion depth. The carina is recommended as a useful target level for CVC tip position. Therefore, if we can place the CVC tip at the level of the carina by using the external landmark, it is very useful. We evaluated the sternal head of right clavicle and the nipples as anatomic landmarks for practically determining the optimal depth of CVC in paediatric patients.

**Methods:** Before the start of this study, to identify the relative positions of the sternal head of right clavicle, the nipples, and the carina, chest radiography (CXR) were taken after attaching the radio-opaque material on the nipples in another 30 paediatric patients under 5 years old. The mean (SD) age, weight and height of pilot patients were 32.6 (24.9) month, 14.0 (7.7) kg and 88.6 (20.6) cm respectively. The data showed that the midpoint on the perpendicular line from the sternal head of right clavicle to a line connecting both nipples was located 0.5 (0.6) cm below the carina.

Ninety children under 5 years old, planned for catheterization through the right internal jugular vein were enrolled. The insertion depth was determined using the puncture site and the external landmarks. Point I (insertion point), A (the sternal head of a right clavicle) and B (the midpoint of the perpendicular line drawn from A to the line joining both nipples) became indicators. The insertion depth of CVC was determined by adding the two distances (from I to A, from A to B) and subtracting 0.5 cm from this. A chest radiography was taken and the distance of CVC tip from the carina level was measured by the Picture Archiving and Communicating System.

**Results:** The mean distance of the CVC tip from the carina level was 0.1 (1.0) ( $P = 0.293$ ) cm above the carina (95% CI 0.1 cm below carina - 0.3 cm above carina). There was no specific relationship between the distance of the CVC tip from the carina level vs. the patients' age, height and weight.

**Conclusions:** CVC tip can be placed near the carina by using the external landmarks without any formulae, images, and devices in children under 5 years old.

PREDICTORS OF EXTUBATION FAILURE IN THE OPERATING ROOM AFTER OFF PUMP CORONARY ARTERY BYPASS GRAFTING.

DORSA A; ROSSI A; LUPIAÑEZ B; NAVIA D; RAICH H; PICCININI F; VACCARINO G; THIERER J; VRANCIC M  
*ICBA*

**INTRODUCTION:** Extubation in the operating room after off pump coronary artery bypass (OPCABG), "Ultra Fast-track" (UFT), is not considered a standard practice of care.

**OBJECTIVE:** To demonstrate the feasibility and safety of UFT in OPCABG and to obtain failure predictors of this strategy.

**MATERIAL AND METHOD:** Prospective Cohort Study. Between 01-01-2004 and 31-12-2007 1196 consecutive patients underwent OPCABG, all subject to UFT. All were placed under general anesthesia and extubated in the operating room following technical criteria as described (1). In all cases patients were approached by median sternotomy and complete revascularization was attained, exclusively with arterial conduits in most cases.

**RESULTS:** 1065 patients (89.05%) were extubated in the operating room. Mean age was 64 years old, and 87% were male. Surgery was elective in 62% of the cases. In 3% an intraaortic balloon pump was placed preoperatively. In multivariate analysis preoperative predictors of UFT failure were reoperation (OR 3.92, 95% CI 2.07-7.41,  $p < 0.001$ ), pre-existing renal disease (OR 3.06, 95% CI 1.62-5.80,  $p < 0.0001$ ), diabetes (OR 1.7 95% CI 1.15-2.51,  $p = 0.007$ ), preoperative use of intraaortic balloon pump (OR 7.37 95% CI 3.54-15.3,  $p < 0.0001$ ) and skin to skin time (OR 3.76 95% CI 1.004-1.01,  $P < 0.0001$ ). Compared with non-extubated patients, patients in whom UFT was feasible presented: lower reintubation rate (2.54% vs. 16.03%,  $p < 0.001$ ), myocardial infarction (1.03% vs. 4.58%,  $p = 0.001$ ), renal insufficiency (2.25% vs. 7.63%  $p < 0.001$ ), stroke (0.38% vs. 2.29%,  $p = 0.032$ ), and perioperative mortality (1.22% vs. 10.69%,  $p < 0.001$ ). Length of hospital stay was also statistically lower: median 6 vs. 7 days  $p < 0.001$ .

**CONCLUSIONS:** UFT is feasible and safe in most patients undergoing OPCABG. Baseline characteristics and surgical variables determine the feasibility of implementing it.

## PREDICTORS OF SUSTAINED REVERSED RADIAL-TO-FEMORAL ARTERIAL PRESSURE GRADIENT ASSOCIATED WITH CARDIOPULMONARY BYPASS IN PATIENTS UNDERGOING VALVULAR HEART SURGERY

Kwak Y; Hong S; Choi Y; Kim J; Chun D; Shim J

*Yonsei University College of Medicine*

**Objective:** Sustained underestimation of the central aortic pressure by the radial arterial pressure commonly develops following cardiopulmonary bypass (CPB), leading to inappropriate use of vasopressors. The aim of this study is to identify clinical predictors leading to a sustained reversed radial-to-femoral arterial pressure gradient (RFPG) in patients undergoing valvular heart surgery (VHS).

**Methods:** Two hundred patients undergoing VHS were prospectively studied. Patients who developed sustained reversed RFPG (systolic RFPG  $\geq$  10 mmHg and/or mean RFPG  $\geq$  5 mmHg) from immediately after discontinuation of CPB until the end of the surgery were compared with patients who did not develop any reversed RFPG.

**Results:** Data from 193 patients were analyzed and 53 (27%) patients developed sustained reversed RFPG, whereas 80 (41%) patients did not develop any RFPG. In univariate analysis, female sex, presence of atrial fibrillation, use of digoxin and diuretics, increased left atrial volume index, decreased right ventricular ejection fraction, increased right ventricular end diastolic and systolic volume index, longer duration of CPB and aortic cross clamping, and use of vasopressors during CPB were identified as risk factors. In multivariate analysis, only preoperative atrial fibrillation and use of diuretics were identified as independent risk factors of the sustained reversed RFPG.

**Conclusion:** In VHS, 27% of patients developed sustained reversed RFPG following CPB. Preoperative atrial fibrillation and use of diuretics were identified as independent risk factors, and monitoring femoral or axillary arterial pressure should be considered in this subset of patients to guide hemodynamic management.

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## PREOP HEPARIN AFTER CLOPIDOGREL INCREASES FIBRINOGEN AND DECREASES POSTOP BLOOD LOSS FOR CABG.

Pothula S; Inchiosa, Jr M; Sanchala V; Rosario M; Liang I; Kubal K; Yap E

*New York Medical College*

**INTRODUCTION:** Treatment of cardiac surgical patients with antiplatelet therapy in the near-preoperative period is known to increase perioperative blood loss (1). It was previously reported that patients who received intravenous heparin in addition to a platelet adenosine diphosphate (ADP) receptor inhibitor, in the preoperative period, showed higher plasma fibrinogen concentrations and reduced blood loss postoperatively (2). The withdrawal of aprotinin (Trasylol) from clinical use in November, 2007, prompted us to examine retrospectively our recent experience with the use of intravenous heparin preoperatively, both with and without clopidogrel (Plavix) therapy.

**METHODS:** With IRB approval and a HIPAA waiver for informed consent, anonymous data were examined from a total of 112 patients who only had CABG surgery and did not receive aprotinin; 52 patients received Plavix alone in the week preceding surgery; 44 received both Plavix and a low-level intravenous heparin infusion (~1000 units/hr) (Plavix +IV Hep group); a third group (16) received only heparin (IV Hep). Plasma fibrinogen at the end of surgery and postoperative blood losses (0-24 hr) were examined for this preliminary report. No distinction was made about the duration of heparin therapy, except that patients receiving less than 24 hours of infusion were omitted.

**RESULTS:** Both the Plavix + IV Hep and the IV-Hep groups showed statistically significant decreases in postoperative blood losses compared with the Plavix group (Fig. 1). Also, the Plavix + IV Hep group had the highest plasma fibrinogen levels postoperatively (Fig. 2). The r-squared value for the correlation between plasma fibrinogen and postoperative blood loss was the strongest (0.763) for the group that received only IV Hep (Fig. 3) ( $P < 0.00003$ ).

**DISCUSSION:** These findings appear to be consistent with those of the previous study (2). One may speculate that the inhibition of thrombin by intravenous heparin decreased the breakdown of fibrinogen, and the increased fibrinogen improved hemostatic competency. This may have translated to a decrease in blood loss in the postoperative period.

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## PREOPERATIVE ACE INHIBITOR USE ATTENUATES HEPARIN-INDUCED HYPOTENSION

Chi J; Ceballos A; Strouch Z; Taneja R; Drum M; Chaney M

*Metropolitan Anesthesia Consultants; University of Chicago Medical Center*

**INTRODUCTION:** Studies have described a sudden decline in MAP in response to large bolus administration of intravenous heparin for cardiac surgery. While no definitive consensus on mechanism exists, it is thought to be caused by a decrease in SVR (1,2). Preoperative use of angiotensin-converting enzyme inhibitors (ACEi) have also been associated with intraoperative hypotension (3) and are commonly used by cardiac surgical patients. The purpose of this prospective, case-controlled, observational study was to determine if preoperative ACEi use exaggerates the hemodynamic response to heparin.

**METHODS:** Following Institutional Review Board approval, adult patients scheduled for cardiac surgery requiring full (300 U/kg) heparinization were recruited. Exclusion criteria included use of preoperative heparin or vasopressor infusions, ventricular-assist devices, IABP, preoperative mechanical ventilation, and trauma or emergency cases. Patients were categorized into two groups: those on preoperative ACEi therapy and those who were not. Anesthetic technique was at the discretion of the anesthesiologist. Measurements included MAP, HR, CVP, PAP, PCWP, and CO. These measurements were taken immediately before heparin administration (baseline) and 1 and 4 minutes thereafter. Any use of vasopressor support around the time of heparin administration was also noted. SVR and PVR were calculated.

**RESULTS:** See Figure 1. Twenty patients were enrolled in each group and they were similar in age, height, weight, and baseline hemodynamic measurements. Important changes (post-heparin) in non-ACEi patients included a significant decrease in SVR and MAP (1 min and 4 min). In contrast, ACEi patients demonstrated a significant decrease in SVR only at 4 min (not at 1 min) and an increase in MAP (not significant). Additional statistically significant differences within groups are noted in Figure 1. The only statistically significant difference between groups was regarding MAP changes (at both times). One patient in the ACEi group and two patients in the non-ACEi group required temporary vasopressor support (phenylephrine or vasopressin).

**DISCUSSION:** Adverse hemodynamic changes have been independently associated with heparin administration and preoperative ACEi use yet no study has attempted to correlate the relationship between the two. Our study indicates that preoperative use of ACEi may have protective effects by attenuating heparin-induced decreases in SVR and MAP. In fact, patients receiving preoperative ACEi had increased MAP post-heparin, perhaps because of the differences between the two groups (post-heparin) regarding HR, SVR, and PVR. This study illustrates the need for further elucidation regarding the physiologic effects of heparin administration and introduces an interesting and clinically important relationship with ACEi.

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PREOPERATIVE HEMOGLOBIN A1C >8 MAY BE A BETTER PREDICTOR THAN HISTORY OF DIABETES MELLITUS OF POSTOPERATIVE TARGET GLYCEMIC RANGE ACHIEVED FOLLOWING CARDIAC SURGERY IN A MULTIVARIATE LINEAR REGRESSION MODEL

Subramaniam B; B A; S D

*Beth Israel Deaconess Medical Center*

Background: An established glycemic protocol is in place in our cardiac surgical units (1). Different protocols achieve a mean target glycemic duration of 60 to 70%. This is influenced by a) patient risk factors, b) surgery type and c) glycemic protocol and d) nursing protocol adherence. In an established set up, the first two factors must play a significant role in determining the target duration. We investigated the role of preoperative Hemoglobin A1C (HbA1C) on the achieved target duration.

Methods: Consecutive patients with their index surgery from first seven months of 2008 were chosen. Society of Thoracic Surgery preoperative covariates were collected along with preoperative HbA1C (within 30 days prior to surgery) level. The intraoperative glycemic control data were not included for this analysis as this has been shown to have lesser influence on patient outcome (2). Patients with completed hourly blood glucose measurements were analyzed. A univariate analysis was done to examine the individual influence of preoperative variables. HbA1C was included both as a continuous variable and as a dichotomous variable (>6 vs. <=6). A multivariate regression model was built with a forward stepwise selection (entry  $p < 0.05$  and removal  $> 0.10$ ). SPSS 15.0 (Cary, NC) was used and  $p < 0.05$  was significant.

Results: 519 primary surgeries were identified. 87% had complete data for the first 48 hours glucose and 70% had preoperative HbA1C. The achieved mean duration was 63% [20%] and was normally distributed. In the univariate analysis, h/o of DM, hypertension, smoking, insulin use and HbA1C>6 were significant predictors of poor mean duration of control. HbA1C and mean duration had a weak negative correlation (-0.24). In an exploratory analysis, 92% had HbA1C <8. Patients with HbA1C >8 (8%) achieved only 49% of mean duration. A Kruskal-Wallis test was done to evaluate the differences between HbA1C groups [ $< 6$  (n=223), 6-7.9 (n=119), 8 to 10 (n=16), >10 (n=11)] ( $p < 0.001$ ). Based on patient numbers and means, they were collapsed into HbA1C <8 or >=8 for multivariate analysis. This revealed,

a) Mean control = 66% + (-10) h/o DM.

b) Mean control= 65% + (-7.5%) h/o DM [ $p < 0.001$ ] + (-8) HbA1C >8 [ $p = 0.05$ ]

c) Mean control= 62% + (-13) HbA1C>8

Confounding and collinearity were addressed (VIF 1.16 is against collinearity). Both positively confound each other and need to be included in the final model. These results need to be confirmed by a prospective collection of HbA1C data and its influence on the duration of control.

Conclusions: HbA1C a) may be a better predictor of achieved target range b) gives incremental value over h/o DM, c) Captures undiagnosed DM. Glycemic variability can be minimized by better duration in the target (3) and various protocols need to be evaluated.

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## PREOPERATIVE LEVELS OF OMEGA FATTY ACIDS ARE ASSOCIATED WITH POSTOPERATIVE DEPRESSIVE SYMPTOMS IN CARDIAC SURGICAL PATIENTS

Phillips-Bute B; James B; Mihai P; Mark N; Joseph M

*Duke University; Duke University Medical Center*

**Introduction:** Research over the past two decades has shown strong associations between depression and cardiac health. Depressed patients are more than twice as likely as non-depressed patients to have a cardiac event within 12 months after cardiac surgery(1) Among cardiac patients, depressed subjects have lower concentrations of omega-3 fatty acids, particularly eicosapentaenoic acid(EPA) and docosahexaenoic acid(DHA), and lower ratios of omega-3 to omega-6 (arachidonic acid) fatty acids. We therefore sought to determine if the preoperative levels of these fatty acids are associated with depressive symptoms at baseline and at 6 weeks after coronary artery bypass graft (CABG) surgery.

**Methods:** Following IRB approval, patients enrolled in prospective trials examining neurocognitive outcomes, completed the Center for Epidemiological Studies Depression questionnaire (CES-D) on the day prior to surgery, and at 6 weeks after surgery. Patients were excluded if they received heparin before surgery, had a history of symptomatic cerebrovascular disease, alcoholism, psychiatric illness, or renal failure, had < 7th grade education, were pregnant, or had a Mini-Mental State Examination score < 24 at baseline. Plasma levels of essential fatty acids including EPA, DHA, and arachidonic acid were measured at baseline by the gas chromatography mass spectroscopy stable isotope dilution method. CES-D scores < 16 defined patients with no depressive symptoms, 16-27 defined patients having moderate depressive symptoms, and scores  $\geq 27$  defined severe depressive symptoms. CABG patients without depressive symptoms were compared to patients who showed either moderate or severe depressive symptoms, both at baseline and at 6 weeks, using the t-test;  $p < 0.05$  was considered significant

**Results:** Our study sample consisted of 47 patients with no depressive symptoms, 24 with moderate symptoms, and 6 with severe symptoms at 6 weeks after surgery. Levels of arachidonic acid were significantly higher at baseline and at 6 weeks in patients with depressive symptoms compared to patients without depressive symptoms (6 weeks: 1112 vs. 975  $\mu\text{mol/L}$ ,  $p = 0.03$ ; Figure 1). DHA, EPA, and DHA/arachidonic acid levels were also lowest among the patients with severe depressive symptoms, but this difference was not statistically significant in the smaller patient sample.

**Conclusions:** To our knowledge, this is the first time that preoperative levels of fatty acids are shown to be associated with postoperative depressive symptoms in cardiac surgical patients. Because fish oil supplementation has been associated with not only increased levels of DHA and EPA, but decreased levels of arachidonic acid(2), our findings suggest the potential benefit of an interventional trial using fish oil to decrease post-operative depression in cardiac surgical patients.

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## PREOPERATIVE RENAL INSUFFICIENCY SEVERITY IS INDEPENDENTLY ASSOCIATED WITH POSTOPERATIVE MORBIDITY FOLLOWING CORONARY ARTERY BYPASS GRAFT SURGERY

Tolpin D; Syed S; Lee V; Elayda M; Collard C; Pan W

*Baylor College of Medicine; Baylor College of Medicine and Texas Heart Institute; Texas Heart Institute; Texas Heart Institute and Baylor College of Medicine*

**Introduction:** Although preoperative renal insufficiency (RI) has been reported to be a risk factor for cardiac surgery, few studies have used glomerular filtration rate (GFR) to define degrees of RI severity.(1,2) We investigated the influence of preoperative RI severity, as defined by GFR, on adverse postoperative outcomes following coronary artery bypass graft (CABG) surgery.

**Methods:** A retrospective cohort study was performed of patients (n=4135) undergoing primary isolated CABG surgery with cardiopulmonary bypass (CPB) between January 2002 and December 2007. Patients were classified into 4 groups: "normal" = GFR  $\geq$  90 ml/min per 1.73 m<sup>2</sup> (n=1119); "mild" RI = GFR 60-89 ml/min per 1.73 m<sup>2</sup> (n=1937); "moderate" RI = GFR 30-59 ml/min per 1.73 m<sup>2</sup> (n=895); and "severe" RI = GFR < 30 ml/min per 1.73 m<sup>2</sup> (n=184). GFR was estimated by the use of the Modification of Diet in Renal Disease study equation.(3) Multivariate, stepwise logistic regression was performed controlling for patient demographics, medical history, preoperative medications and intraoperative risk factors to determine if preoperative RI severity was independently associated with worsened postoperative outcomes.

**Results:** Postoperative outcome indices and hospital length of stay (HLOS) for each group are presented in Table 1. Multivariate stepwise logistic regression demonstrated that mild RI was independently associated with an increased risk of postoperative ventilator dependence (OR=2.2; 95% CI=1.3 to 3.8; P<0.01), ventricular tachycardia (OR=1.5; 95% CI=1.1 to 2.2; P<0.05) and sternal wound infection (OR=5.7; 95% CI=1.3 to 24.8; P<0.05). In contrast, moderate RI was independently associated with worsened postoperative morbidity and mortality, including 30-day all-cause of mortality (OR=3.1; 95% CI=1.5 to 6.0; P<0.01), cardiac arrest (OR=1.7; 95% CI=1.0 to 2.6; P<0.05), use of intra-aortic balloon pump after CPB (OR=1.7; 95% CI=1.1 to 2.7; P<0.05), sternal wound infection (OR=5.5; 95% CI=1.2 to 25.3; P<0.05), and prolonged HLOS (p<0.05). The incidences of these and other outcomes were even higher in patients with severe preoperative RI (Fig. 1).

**Conclusion:** Preoperative RI is independently associated with postoperative mortality and morbidity following CABG surgery. Moreover, postoperative mortality and morbidity is directly proportional to preoperative RI severity.

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## PULMONARY VENOUS FLOW PROFILES OBTAINED FROM INTRAOPERATIVE TEE ARE USEFUL FOR DECIDING THE SIZE OF THE BAND FOR BILATERAL PULMONARY ARTERY BANDING.

Kurokawa S; Tomita Y; Onuki E; Seino Y; Nomura M; Ozaki M

*Tokyo Women's Medical University*

### Introduction

Bilateral pulmonary artery banding (bil.PAB) is now being applied, in combination with steps to maintain the patency of ductus arteriosus, for the control of pulmonary blood flow (PBF) and maintenance of systemic circulation in patients with hypoplastic left heart syndrome (HLHS) or other lesions with hemodynamics similar to those of HLHS (HLHS variant).

Some investigators have reported that optimal banding on each side requires a PAB flow with a peak velocity of more than 3.0 m/sec on epicardial echography. Notwithstanding, compression of PA can influence the flow profiles in this way.

Based on our previous experiences with conventional PAB, we assume that reduction of PV return can serve as a marker for optimal PAB. The aim of this study is to investigate whether TEE can help guide decisions on the optimal size of the band for bil.PAB.

### Methods

Six patients who underwent bil.PAB, including one who underwent the procedure twice, were enrolled in this study. The marker for optimal PAB was defined as a reduction of mean velocity (m-V) of pulmonary vein (PV) flow to approximately 50 to 60% of the pre-PAB value. PAB was achieved by snaring each PA with strings in the first 2 cases and by fastening each PA with strips of artificial graft in the other 4 cases. The size of the band was adjusted by either snaring the PA tightly or by tightening incrementally with additional stitches, until m-V was reduced to within the target range. Next, bilateral PAB flows were detected to measure the peak velocities after completion of bil.PAB procedure. Spearman's rank correlation was used for statistical analysis, and  $p < 0.05$  was considered significant.

### Results

The patients ranged from 4 days to 2 months in age and from 2.4 kg to 3.0 kg in weight. One case was diagnosed as HLHS and the others were diagnosed as HLHS variants. The bilateral PV return could be visualized throughout all 7 bil.PAB interventions in spite of adjustment procedures, enabling us to evaluate the size of the band by our method. The m-Vs were actually reduced to 50 to 80% of the pre-value. Unlike the PV flow, the PAB flow was not feasibly detectable, and the rate of detection was lower on the left side (4/7) than on right side (6/7). There was no correlation between the reduction of m-V and peak velocity of the PAB flow. The PAB flow exceeded 3.0 m/sec in the 3 out of 7 PABs, in which the targeted range of m-V was reached. However, all but one of the cases reached the second-stage operations without any intervention. The one exception showed only a 20% of reduction of the left-sided PV return, and thus required a re-bil.PAB 2 days after the first bil.PAB. Ventricular distension was frequently seen during left PA exposure because of severe decompression of the main PA trunk. The incidence of sudden disruption of PBF immediately after banding was markedly higher than that during conventional PAB (in 6/14 versus 2/15 PABs).

### Conclusion

In conclusion, intraoperative TEE evaluation focusing on PV return can be of use for deciding the size of the band during bil.PAB. Reduction of PV return to 50 to 60% of pre-value can be a marker for optimal banding in bil.PAB. TEE is also useful for avoiding deterioration of ventricular function and unbalanced PBF.

## QUANTIFICATION OF LV VOLUMES AND EJECTION FRACTION BY 3D TRANSESOPHAGEAL ECHOCARDIOGRAPHY: INTRA- AND INTEROBSERVER VARIABILITY.

Phillips-Bute B; de Lange F; Rivera D; Mackensen G; Swaminathan M

*Duke University Medical Center*

**Background:** The perioperative assessment of left ventricular (LV) volumes and ejection fraction (EF) is important to quantify LV function. Although LV function is routinely assessed using two-dimensional transesophageal echocardiography (2D-TEE), studies suggest limitations due to image quality, foreshortening and geometric assumptions regarding volume calculation. The introduction of three-dimensional TEE (3D-TEE) along with a semiautomated endocardial border detection system presents a promising technology to obtain fast and objective measurements for global LV function and volumes based on a 3D data set. While the technology may facilitate accurate assessment of LV function for the less experienced echocardiographer, the required level of experience and reproducibility are unknown. Therefore, we evaluated the intra- and inter-observer variability of LV 3D-TEE assessments performed by an experienced and a novice echocardiographer.

**Methods:** With IRB approval, 3D-TEE full volume loops from 50 patients undergoing cardiac surgery were studied. All patients underwent a comprehensive TEE evaluation including standard 2D as well as the 3D assessment with the real-time 3D-TEE Matrix transducer (iE33 system; Philips Medical Systems). Digitized images independently were assessed off-line by two observers, one novice (OBS1) and one experienced board-certified echocardiographer (OBS2), using built-in software (QLAB 6.0). Enddiastolic (EDV), endsystolic (ESV) LV volumes, EF and time needed to perform the assessment were noted. Based on these data, an intra- and inter-observer correlation was obtained and a Bland-Altman analysis performed.

**Results:** Intra-observer variability was low with excellent correlations in both the novice OBS1 (Pearson coefficient  $r=0.98$  for EDV,  $0.98$  for ESV and  $0.93$  for EF) as well as in the experienced OBS2 ( $r=0.98$  for EDV,  $0.97$  for ESV and  $0.91$  for EF). Average time needed for the assessment was  $165s (\pm 73)$  for OBS1 and  $130s (\pm 63)$  for OBS2 ( $p < 0.001$ ).

Inter-observer correlation was high for EDV and ESV ( $r=0.97$  for EDV,  $0.94$  for ESV) and moderately high for EF ( $r=0.78$ , figure 1A), with an average absolute difference in EF of  $7.8\% (\pm 7.3)$ . Bland-Altman analysis revealed no bias towards one observer (Figure 1B).

**Conclusion:** Our study shows that both novice and experienced observers can reproducibly determine LV volumes and EF based on 3D-TEE data using built-in software. The correlation between observers was particularly high for volume assessments, indicating that this tool, even for the non-experienced operator, may prove useful for noninvasive perioperative quantification of LV volumes. There was reasonable correlation for EF between the observers. This information, along with studies demonstrating greater accuracy of 3D versus 2D LV evaluation, suggests that 3D-TEE assessment offers accurate and reproducible perioperative quantification of LV volumes and EF for both experienced and inexperienced users.

## QUANTIFICATION OF THE GEOMETRY OF NORMAL MITRAL VALVES COMPARED TO VALVES WITH POSTERIOR LEAFLET PROLAPSE USING REAL TIME THREE-DIMENSIONAL TRANSESOPHAGEAL ECHOCARDIOGRAPHY

Shull R; Weitzel N; Puskas F; Seres T

*University of Colorado Health Science Center*

### Objective:

Using real time three-dimensional transesophageal echocardiography (RT-3D-TEE) and the Mitral Valve Quantification (MVQ) software package (Philips Medical Systems), we compared parameters of normal mitral valves with those that had posterior leaflet prolapse and underwent repair.

### Methods:

Normal mitral valves of 20 patients undergoing procedures involving cardiopulmonary bypass were evaluated and quantified with RT-3D-TEE using full volume images and the MVQ software. Pre- and post-bypass studies were performed on each valve. Normal mitral valves were identified as having trace or less regurgitation using two-dimensional imaging with color flow Doppler. Four patients with posterior mitral leaflet prolapse scheduled for mitral valve repair were evaluated pre- and post-repair. All mitral valves in this study were evaluated at end systole. The intercommissural (IC) and anterior-posterior (AP) diameter, annular circumference, anterior and posterior leaflet area, volume of leaflet prolapse, and the length of coaptation were quantified.

### Results:

The normal mitral valve parameters did not change significantly from the pre- and post-bypass exams (first rows of Table 1 and 2). The remodeling of the mitral valve in cases of posterior leaflet prolapse caused significant changes in IC and AP diameter, annular circumference, posterior leaflet area, volume of prolapse, and the length of coaptation when compared to normal valves in the pre-bypass period (Table 1). The parameters of the repaired valves were not significantly different from the normal valves in the post-bypass period (Table 2) except for the shorter length of coaptation. Furthermore, posterior leaflet prolapses can be localized with great accuracy with this technique (see arrow in image).

### Conclusion:

The use of RT-3D-TEE imaging with mitral valve quantification provides detailed information about mitral valve geometry. The 20 normal valves examined in this study had similar values pre- and post-bypass which suggests that the technique is consistent and there is no significant changes in mitral valve geometry during cardiopulmonary bypass. With the knowledge of normal mitral valve anatomy, the prolapses of posterior leaflets can be characterized and the changes with repair can be evaluated. This technique has the potential to more accurately localize prolapsed segments when compared to two-dimensional imaging and can be applied to a wide range of mitral pathologies. Continued experience could allow it to become an integral part of surgical decision making.

## REAL TIME 3D TEE IS SUPERIOR TO 2D TEE IN EXACT LOCALISATION OF INVOLVED SEGMENTS IN MITRAL VALVE REGURGITATION

Ender J; Schlegel M; Wittmann M; Koncar-Zeh J; Mukherjee C

*Heartcenter University Leipzig*

**Introduction:** Segmental analysis with echocardiography in patients undergoing mitral valve repair is essential for successful treatment. Aim of our study was to investigate the additional value of Real time 3D transesophageal echocardiography (RT3D) as compared to conventional 2D TEE in patients undergoing elective mitral valve repair.

**Methods:** After approval of the local ethic committee and written informed consent patients undergoing elective mitral valve repair were included in this prospective study. After induction of anesthesia a comprehensive 2D TEE examination was performed by an experienced echocardiographer using the ASE/SCA guidelines (1). At the end each segment of the mitral valve (A1,A2,A3,P1,P2,P3, anterior commissure(AC), posterior commissure (PC)) was judged as normal, prolapsing or restrictive. Then RT3D with the 3D -Zoom mode was used to evaluate the different segments of the mitral valve. Additionally the underlying pathology was determined using the Carpentier classification according to the movement of the leaflets with Type I for normal, Type II for excessive and Typ III for restrictive (Type IIIa functional and Type IIIb functional) movement. The surgical finding was used as the gold standard for segmental analysis. Only these segments which were surgically corrected either by resection or by implantation of artificial chords were judged pathologic. Agreement with the surgical finding is expressed as percentage.

**Results:** 50 patients were included in this study. Pathology based on the Carpentier classification was type I in 5, type II in 44 patients and type IIIb in 1 patient. Pathology was determined correctly in all patients by RT 3D and in 48 patients by 2DTEE. In two patients with a cleft in the anterior leaflet the diagnosis was missed by 2 D TEE. Segmental analysis and agreement with the surgical finding is shown in table 1.

**Conclusion:** RT 3D TEE is superior to 2D TEE in segmental analysis of the mitral valve as well as in detecting cleft-pathology in patients undergoing mitral valve repair for mitral regurgitation.

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## REGIONAL WALL MOTION EVALUATION DURING CARDIAC SURGERY: THE IMPORTANCE OF SPECKLE TRACKING ECHOCARDIOGRAPHY

Skubas N; Kerwick P; Vladagina O; Fontes M

*Weill Cornell Medical College*

### Introduction:

Regional wall motion is evaluated by echocardiographic assessment of inward thickening. This qualitative approach is subjective and considers motion along a single dimension (transverse or radial) only(1). Newer echocardiographic modalities quantify cardiac motion in longitudinal as well as radial dimension by measuring regional systolic velocity (S') with Doppler Tissue Imaging (DTI) or systolic deformation (strain) with Doppler Strain Echocardiography (DSE) or Speckle Tracking Echocardiography (STE)(2-3). The purpose of this pilot project was to examine the incremental value of DTI, DSE and STE in quantifying regional wall motion intraoperatively.

### Methods:

Thirteen patients undergoing elective coronary artery bypass grafting of the right coronary artery were prospectively included. Transesophageal echocardiographic (TEE) examination of the basal inferior segment was done in the mid esophageal 2 chamber view prior to surgical incision (PRE) and immediately after sternal closure (POST). All variables, S'(spectral DTI) and strain (DSE and STE) were measured from the same view. Measurements were done off-line and in triplicate and values were averaged. Results are shown in the table. Statistical analysis included t-test and correlation analysis, with  $p < 0.05$  being significant.

### Discussion:

Whereas peak S' velocity remained unchanged, strain was reduced postoperatively. Doppler (DSE) and non-Doppler (STE) longitudinal strain correlated with each other intraoperatively. This is due to the fact that DTI measurements are subject to translation motion and tethering from adjacent myocardial segments, while strain measures true local deformation. Postoperatively, STE transverse strain was inversely related to longitudinal strain. This may represent a compensatory mechanism, whereas the circumferential myocardial fibers compensate for the decreased function of the longitudinal fibers(4). This theory deserves further exploration. STE is a non-Doppler technique, which is able to discriminate changes in regional strain along different axes. Although only DTI-S' and DSE-strain are available "live", STE may provide more reliable evidence of regional changes.

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## RELATIONSHIP BETWEEN EARLY POSTOPERATIVE PULMONARY DYSFUNCTION AND MORTALITY AFTER CORONARY ARTERY BYPASS GRAFTING

Cuthbert Hudson J; Stafford Smith M; Phillips-Bute B; Hudson C; Young C; Gaca J; Welsby I; Bartz R

*Duke University; VAMC*

### Intro:

Acute respiratory distress syndrome (ARDS) is highly associated with morbidity and mortality following aortocoronary bypass (CABG) surgery,<sup>(1)</sup> but the relationship between less severe pulmonary dysfunction and outcome is poorly understood. Therefore, we tested the hypothesis that postoperative pulmonary dysfunction, using a more liberal definition than ARDS alone, is associated with worsened 30 day mortality and long-term survival after cardiac surgery.

### Methods:

With IRB approval, 5683 consecutive CABG surgery patients between Sep93 to Jun01 were included for analysis in this retrospective observational study. Patients undergoing off-pump or valvular surgery were excluded. Pulmonary dysfunction was defined as postoperative pulmonary edema, pneumonia, and/or ARDS. Secondary analyses of ventilatory failure considered postoperative ventilation requirements greater than 24 and 48 hours. Long-term survival was examined with the Kaplan-Meier survival analysis. Hazard ratios were calculated using Cox proportional hazard models.  $P < 0.05$  was considered significant.

### Results:

Demographics were similar to those seen in other studies.<sup>(1)</sup> Incidence rates for pulmonary edema, pneumonia, and ARDS were 7.9%, 1.6%, and 0.5%, respectively. Median follow-up time was 1009 days. Patients with postoperative pulmonary dysfunction had higher 30-day mortality rates (6.2 vs. 2.2%;  $p < 0.0001$ ), and worsened long-term survival (hazard ratio 1.98;  $p < 0.0001$ ). Patients ventilated longer than 24 and 48 hours had higher 30-day mortality rates (7.2% and 12.6% respectively;  $p < 0.0001$ ) than patients ventilated less than 24 hours (2.24%;  $p < 0.0001$ ). Patients ventilated greater than 24 or 48 hours were less likely to survive long term (hazard ratios 2.32 and 3.29, respectively;  $p < 0.0001$ ). Individually, pulmonary edema, pneumonia, and ARDS were all associated with increased 30-day mortality, with rates of 4.9%, 18.5%, and 20%, respectively. Similar relationships were observed with long-term mortality (figure).

### Conclusion:

Postoperative pulmonary dysfunction is strongly associated with both worsened 30-day mortality and long-term survival following CABG surgery. This is true whether lung dysfunction is characterized by pulmonary condition (pulmonary edema, pneumonia or ARDS) or requirement for ventilatory support (24 or 48h postoperatively). Further investigation to characterize predictors of pulmonary dysfunction and potential protective strategies may improve cardiac surgery outcomes.

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## RESTRICTIVE LUNG DISEASE INCREASES THE RATE OF RESPIRATORY FAILURE AFTER BILATERAL ORTHOTOPIC LUNG TRANSPLANTATION

Pabich W; Welsby I; Balsara K; Bush E; Lee S; Phillips-Bute B; Davis R; Lin S

*Duke University*

### INTRODUCTION:

Restrictive lung diseases (RLD) caused by idiopathic pulmonary fibrosis (IPF), sarcoidosis, and collagen vascular diseases alter chest wall mechanics impairing postoperative respiratory function after bilateral orthotopic lung transplant (BOLT). This is increasingly important as RLD has an increasing incidence of 30/100,000 patients, and lung transplants for IPF alone are the second most common reason BOLT is performed[SPCHAR(sub1)]. Still, it remains unclear if patients receiving BOLT for RLD have a higher rate of postoperative respiratory failure. We hypothesize that patients with RLD have increased postoperative respiratory failure and, that patient characteristics are associated with increased respiratory failure.

### METHODS:

After IRB approval was obtained, we completed a retrospective review of adult, primary off pump-BOLTs performed between 1/2000 and 1/2006 at a single university center (n=198). Patients were divided into three disease categories: RLD (including IPF and sarcoidosis), cystic fibrosis (CF), and chronic obstructive pulmonary disease (COPD). Perioperative deaths (n=5) were excluded from analysis. We used postoperative tracheostomy (trach) as a marker of respiratory failure. Donor and RLD recipient characteristics were compared for those with and without respiratory failure (Table 1). PaO<sub>2</sub>-to-FiO<sub>2</sub> (PF) ratio is a marker of graft dysfunction, BSA is body surface area, and custom antibiotics were used for patients colonized with resistant organisms. Statistical analyses were performed using the Chi-squared and Wilcoxon rank sum tests.

### RESULTS:

When compared to other disease processes, there is a greater incidence of postoperative respiratory failure after BOLT requiring trach amongst the RLD population (Chi-squared statistic; p=0.004). Moreover, independent risk factors for trach amongst the RLD population include female gender (p=0.005) and total perioperative blood products transfused (p=0.005).

### CONCLUSION:

We observed more respiratory failure after BOLT in RLD patients, which is more common in female recipients and those receiving more blood transfusion. The latter may be a marker for operative difficulty, as respiratory failure does not appear to be related to graft dysfunction in terms of poor oxygenation, which is how transfusion related lung injury would present. This may, therefore, be more readily explained by unique mechanical disturbances of the chest wall in patients with RLD, and efforts should be directed towards predicting patients who would benefit from early trach to facilitate their postoperative recovery.

### REFERENCES:

[SPCHAR(sub1)]J Heart Lung Transplant. 2008 Sep;27(9):957-69.

## RIGHT VENTRICLE DYSFUNCTION - ROLE OF INTRAAORTIC BALLOON COUNTERPULSATION AND VASOPRESSOR THERAPY

Ho J; Liakopoulos O; Buckberg G; Sanchez E; Crowley R; Mahajan A

*David Geffen School of Medicine at UCLA*

**Objective:** Experimental direct augmentation of right coronary perfusion improves right ventricular (RV) dynamics following high afterload RV failure, but is not clinically feasible. Increasing coronary perfusion pressure (CPP) using high dose vasoconstrictors has yielded mixed result in laboratory settings and can lead to afterload-induced LV dysfunction. The addition of intraaortic balloon pump (IABP) therapy to vasopressor may yield better results due to augmented CPP and LV afterload reduction. This study shows IABP in combination with vasopressor infusion favorably treats RV failure and is superior to either therapy alone.

**Methods:** In 10 anesthetized pigs, RV failure was induced by pulmonary artery constriction and systemic hypertension strategies with IABP, phenylephrine (PE) or the combination of both were tested. Systemic and ventricular hemodynamics (cardiac index (CI), ventricular pressures, CPP) were measured and echocardiography was used to assess tricuspid valve regurgitation, septal positioning (eccentricity index (ECI)), and changes in ventricular and septal dimensions and function (myocardial performance index (MPI), peak longitudinal strain).

**Results:** Pulmonary artery constriction resulted in doubling of RV systolic pressure ( $54 \pm 4$  mmHg), RV distension, increased TR (3-4+) with decreased RV function, leftward septal shift (ECI: 1.36;  $p < 0.05$ ), resulting in global hemodynamic deterioration (CI: -51%; SvO<sub>2</sub>: -26%) and impaired CPP (-30%;  $p < 0.05$ ). IABP support alone failed to improve RV function despite higher CPP (+33%;  $p < 0.05$ ). Systemic hypertension by PE improved CPP (+70%), RV function, septal positioning (ECI: 1.12) and minimized TR, but LV dysfunction occurred. With IABP + PE, less PE (-41%) was needed to maintain hypertension and CPP was further augmented (+25%;  $p < 0.05$ ). IABP + PE resulted in LV unloading and restored LV function, and increased CI (+46%) and SvO<sub>2</sub> (+29%;  $p < 0.05$ ).

**Conclusion:** IABP with minimal vasopressors augments coronary perfusion pressure and optimizes biventricular and septal geometry and function thereby resulting in improved RV function after pressure-induced failure.

## RISK FACTORS OF ATRIAL FIBRILLATION FOLLOWING OFF-PUMP CORONARY ARTERY BYPASS GRAFT SURGERY: PREDICTIVE VALUE OF C-REACTIVE PROTEIN AND TRANSFUSION

Shim J; Choi Y; Kim J; Chun D; Hong S; Kwak Y

*Yonsei University College of Medicine*

**Objectives:** Identification of predictors of postoperative atrial fibrillation (AF) would lead to more targeted preventive interventions. In the absence of cardiopulmonary bypass, a specific activator of the inflammatory response, the patient's preoperative inflammatory status and transfusion requirement before the onset of AF would be the key factors among the nonspecific activators influencing the development of AF following off-pump coronary bypass surgery (OPCAB). However, no comprehensive data exist regarding the clinical predictors of AF after OPCAB encompassing these two factors. The aim of this study was to investigate perioperative risk factors of AF, as well as to validate the predictive value of preoperative high sensitive CRP (hsCRP) level and perioperative transfusion requirement for AF following OPCAB in a prospective and observational trial.

**Methods:** Three hundred and fifteen consecutive patients with normal sinus rhythm (NSR) scheduled for isolated OPCAB were prospectively studied. The patients were allocated into either NSR or AF group according to their postoperative rhythm and patients' characteristics, perioperative data including hsCRP level and transfusion requirement were compared. Univariate and multivariate analysis were performed to analyze the risk factors of postoperative AF.

**Results:** AF developed in 66 patients (19%) mostly on the second postoperative day. Patients in the AF group were significantly older and had greater incidence of pre-existing chronic renal failure, which were also identified as risk factors in univariate analysis. Multivariate analysis identified the preoperative highest hsCRP level tertile (adjusted odds ratio 2.2), and perioperative transfusion requirement (adjusted odds ratio 12.7) as independent predictors of postoperative AF. The incidence of AF was proportionally increased according to the increase in the amount of perioperative transfusion and the increase in baseline hsCRP tertile with statistical significance (P for trend < 0.001 and P for trend = 0.032, respectively).

**Conclusion:** The highest preoperative CRP tertile and perioperative transfusion requirement were independent predictors of postoperative AF following OPCAB. Based on these results, preventive measures should be considered in this subset of patients undergoing OPCAB.

### References

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## SELECTIVE DEPLETION OF MICROGLIA USING INTRAPARENCHYMAL CLODRONATE: PRELIMINARY EFFECTS IN HYPOTHERMIC CIRCULATORY ARREST IN RATS

Drabek T; Stezoski J; Jackson E; Janesko-Feldman K; End B; Tisherman S; Kochanek P

*University of Pittsburgh*

**Background:** Prolonged cardiac arrest (CA) produces neuronal death that is associated with microglial proliferation and activation. Microglia, the resident immunocompetent cells in the brain, may contribute to delayed neuronal death, most likely through releasing neurotoxins, including oxygen radicals, and pro-inflammatory cytokines. Microglial activation could contribute to synaptic injury and/or neuronal dysfunction. Microglia could also have a protective role, possibly in delayed repair via elaboration of growth factors. Their proliferation could also represent an epiphenomenon. Thus, there may be benefit from early inhibition or delayed augmentation of microglia. Pharmacological modulation of microglia may improve outcome following CA. Liposome-encapsulated clodronate is a pro-drug that, when injected systemically, depletes macrophages. In this feasibility study, we hypothesized that direct injection of clodronate into the hippocampus would attenuate local microglial proliferation after hypothermic CA in rats.

**Methods:** Isoflurane-anesthetized male adult rats (n=6) were stereotactically administered 5  $\mu$ L of liposome-encapsulated clodronate or liposome-encapsulated PBS into the right or left hippocampus. Rats were then allowed to recover and were returned to the cage. 24 h later, rats were subjected to rapid exsanguination followed by 6 min of CA. Hypothermia was achieved with a flush of ice-cold Plasmalyte (270 ml) into the aorta. After a total of 20 min CA, resuscitation was achieved with cardiopulmonary bypass. Neuropathology was assessed on day 7 using anti-Iba1 staining to detect microglia and Fluoro-Jade C (FJC) to detect neuronal death in both hippocampi. Each rat served as its own control.

**Results:** During CA, the temperature decreased to  $21.3 \pm 2.6$  °C. All rats survived and resumed normal behavior. The number of microglia in hippocampus was decreased in the hemisphere injected with clodronate vs. PBS ( $168 \pm 61$  vs.  $253 \pm 67$ ,  $p < 0.05$ ). The number of FJC-positive neurons did not differ between hemispheres (clodronate,  $153 \pm 39$  vs. PBS  $149 \pm 26$ , respectively;  $p = 0.81$ ).

**Discussion:** The role of microglia in neuroinflammation remains poorly defined. Minocycline administration that attenuated microglial activation showed benefit in neuroinflammatory diseases. In contrast, ablation of microglia in transgenic mice in stroke ischemia models showed detrimental effects. We specifically targeted microglia with clodronate. In this feasibility trial, we have shown that pre-treatment with direct injection of clodronate into the brain attenuates local microglial activation in hippocampus by  $\sim 34\%$ . However, this effect did not alter neuronal death. This suggests that microglia do not play a pivotal role in mediating neuronal death. However, clodronate did not cause total ablation of microglial activity. Also, our insult produced marked loss of neurons and thus we cannot rule out the possibility that depletion of microglia was deleterious, or that the insult was too severe for clodronate to have an impact. This novel strategy provides us with a tool to study the effects of microglia comprehensively in hypothermic CA.

**Support:** Dept. of Anesthesiology, Univ. of Pittsburgh (TD), Society of Cardiovascular Anesthesiologists (TD), NS 38087 and NS 30318 (PMK).

## SIMULTANEOUS COMPARISON OF FORE-SIGHT AND INVOS CEREBRAL OXIMETERS TO JUGULAR BULB AND ARTERIAL CO-OXIMETRY MEASUREMENTS IN HEALTHY VOLUNTEERS

MacLeod D; Ikeda K; Vacchiano C

*Duke University Medical Center; Duke University School of Nursing*

**Introduction:** The purpose of this study is to compare simultaneous measurements from two FDA-approved near-infrared spectroscopy (NIRS) cerebral oximeters: FORE-SIGHT® (CAS Medical Systems, Branford CT USA), and INVOS® 5100 (Somanetics Corp., Troy MI USA) against the commonly used gold standard of weighted co-oximetry jugular bulb and arterial oxygen saturation values during episodes of deliberate oxygen desaturation.

**Methods:** Healthy adult subjects were enrolled in this volunteer study after obtaining written informed consent. A right internal jugular bulb catheter and a left radial arterial line were placed. FORE-SIGHT and INVOS adult sensors were placed on the right & left forehead respectively. A Sequential Gas Delivery system (Respiract, Thornhill Research, Toronto, Canada) was used to deliver gas mixtures following a protocol of step changes of room air, 21%, 8%, 21%, & 50% inspired oxygen at five minute intervals. Oxygen saturation (SpO<sub>2</sub>) was maintained >70% when measured at the finger. Blood samples were drawn simultaneously from the jugular bulb (SjbO<sub>2</sub>) and radial arterial (SaO<sub>2</sub>) catheters and analyzed for oxygen tension using a co-oximeter (GEM 4000, IL, Lexington MA USA). Co-oximeter reference values, CX(F) and CX(I), were calculated based upon previous validation studies of each monitor:  $CX(F) = 0.3 \times SaO_2 + 0.7 \times SjbO_2$ ;  $CX(I) = 0.25 \times SaO_2 + 0.75 \times SjbO_2$ .

Absolute NIRS-derived cerebral tissue oxygen saturation values determined by the FORE-SIGHT (SctO<sub>2</sub>) and INVOS (rSO<sub>2</sub>) monitors were modeled as a function of CX(F) and CX(I) using linear regression. Bias and precision (1 standard deviation) were also determined.

**Results:** Nine subjects (6 male/3 female; 7 Caucasian/2 African American; Age: 21-34 y; weight 56-95 kg) completed the study protocol. A total of 43 samples were analyzed. PaO<sub>2</sub> ranged from 38 - 449 mmHg; PjbO<sub>2</sub> ranged from 25 - 63 mmHg and PaCO<sub>2</sub> ranged from 31 - 53 mmHg. The range of baseline room air values for FORE-SIGHT SctO<sub>2</sub> was 68-76% and for INVOS rSO<sub>2</sub> was 48-87%. The range of baseline room air reference values for CX(F) was 71-80% and for CX(I) was 69-79%. Regression lines for absolute cerebral tissue oxygen saturation values against co-oximeter reference values are shown in Figure 1.

**Conclusion:** The results demonstrate that the FORE-SIGHT cerebral oximeter monitor has greater precision with respect to measuring absolute cerebral tissue oxygen saturation than the INVOS cerebral oximeter monitor.

## TELE-EDUCATION IN CARDIAC ANAESTHESIA / INTENSIVE CARE

Kanchi M; Banakal S; Shetty D

*Narayana Hrudayalaya*

### Objectives:

E-health is the application of information and telecommunication technology for managing and delivering health care services. We have used the tele-medicine facility to conduct academic teaching / training sessions in cardiac anaesthesia. The objective of this study was to examine the feasibility, advantages and disadvantages of this method of tele-learning sessions.

### Methods:

Two base cardiac hospitals with facilities of tele-cardiology link up were established in June 2001. These base hospitals were connected to coronary care unit facilities at six rural area settings. Patients related information (ECG, chest X-ray, echocardiography & coronary angiogram) was transmitted over telecommunication infrastructure and was supported by video- conferencing. Having established the tele- medicine network, the same facility was used to conduct teaching programmes. The teaching / learning session were organized twice a week between the two teaching hospitals. The success of academic session were analyzed in terms of satisfaction of the participating candidates, infrastructural difficulties, if any and the over all outcome of the programme. A questionnaire was formatted and feedback from the participants was obtained. One thousand responses were analyzed and data were tabulated.

### Results:

A total of 293 academic sessions were held in the last three years. Presentation time was 35 minutes in each session and made on a power point. Presentations were followed by discussion. All the participants expressed satisfaction over the teaching and the attendance was 80%.

### Conclusion:

We have found that telemedicine proved to be effective in establishing communication not only between the patient & the physician but also between the teacher and the taught. Several candidates were benefited by this technology. Candidates expressed satisfaction and were content with the teaching methods adapted.

## TEMPORALLY AND REGIONALLY DISPARATE DIFFERENCES IN PLASMIN ACTIVITY BY TRANEXAMIC ACID

Reust D; Reeves S; Abernathy, III J; Dixon J; Gaillard W; Mukherjee R; Koval C; Stroud R; Spinale F

*Medical University of South Carolina*

**Background:** A major complication associated with cardiac surgery is excessive and prolonged bleeding in the perioperative period. Improving coagulation by inhibiting fibrinolysis, primarily through inhibition of plasmin activity (PLact) has been a pharmacological mainstay in cardiac surgical patients. Aprotinin is effective in PLact inhibition, but its withdrawal from the market has resulted in a greater use of tranexamic acid (TXA) which reduces PLact by a different biochemical pathway. The temporal and regional profiles by which TXA modulates PLact remain unexplored. Accordingly, the present study developed a fluorogenic-microdialysis system to measure in-vivo dynamic changes in PLact following TXA administration in a large animal model.

**Methods:** Pigs (~30kg) were randomly assigned to receive TXA (30mg/kg; n=9) or vehicle (n=7) in which microdialysis probes (CMA/Microdialysis, membrane OD=0.5mm) were placed in the right lobe of the liver, anterior myocardium of the left ventricle, right lower pole of the kidney and left quadriceps muscle. The microdialysate infusion (6 uL/min) contained a validated fluorogenic peptide (Sigma A-8171, 0.01mM) which when specifically cleaved by plasmin, yielded a fluorescent moiety (excitation/emission  $\lambda_{max}$ =365/440nm). The relative fluorescence of the interstitial fluid collected from the microdialysis probes, which directly reflected PLact, was determined at steady-state baseline, 30, 60, 90 and 120 minutes following TXA/vehicle infusion. Plasma PLact was determined at the same time points using the same fluorogenic substrate approach.

**Results:** (Figure) With respect to vehicle values, TXA reduced plasma PLact at 30 minutes post infusion ( $p < 0.05$ ). However, temporal and regional differences in PLact were observed following TXA administration. Specifically, there was a consistent and significant ( $p < 0.05$ ) decrease in liver PLact at 90 and 120 minutes post TXA infusion. This liver PLact occurred 60 minutes after the maximal decline in plasma PLact. In contrast, kidney, heart, and quadriceps PLact transiently increased followed by an overall decrease at 120 minutes.

**Conclusions:** Using a large animal model and in-vivo microdialysis measurements of plasmin activity, the unique findings from this study were 2-fold. First, TXA induced a temporally distinct plasmin inhibitory profile within the plasma and interstitial spaces. Second, TXA caused a region specific change in plasmin inhibitory profiles. These temporal and regional differences in the effects of TXA may have important therapeutic considerations when managing fibrinolysis in the perioperative period.

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## THE EFFECT OF CONTINUOUS MONITORING OF STROKE VOLUME BY ARTERIAL WAVEFORM ANALYSIS ON FLUID MANAGEMENT IN HEAD AND NECK RECONSTRUCTIVE SURGERY.

Ralph G; Nicholas M; Minkovich L; Patel R; McCluskey S

*Toronto General Hospital, UHN, University of Toronto*

Wide excision of head and neck cancer with microsurgical free flap's reconstruction (FFR) results to a high cancer cure rate and a good functional recovery. However, this long complex procedure is accompanied with considerable morbidity and mortality. Excessive fluid administration during FFR has been associated with poor outcome(1,2). There is growing evidence that goal-directed fluid therapy might improve outcomes in high-risk patients. The object of the study was to determine the effect of the continuous monitoring of stroke volume (SV) on the intra-operative fluid therapy in FFR.

After obtaining informed consent, 11 patients undergoing FFR for head and neck cancers were enrolled in the study. The standard radial arterial line was connected to FloTrac / Vigileo™ (Edwards Lifesciences, Irvine, CA) that continuously determines SV by analyzing of arterial BP waveforms.

A Volume Loading Step-VLS (250 ml of HES Pentaspan™) was administered. If the SV increased more than 10% after VLS, the patient was considered to be a positive fluids responder. Then, the VLS were repeated until increment in SV had been less than 10% after the prior VLS. This maximal value of SV was obtained as a result of the fluid's loading was considered as optimized, and used as a set point for further fluid therapy. Once optimized, intravascular volume was maintained with continuous infusion of 0.5 ml/kg/hr of Ringer's Lactate. No additional fluid boluses were given until SV decreases by 30% from the maximal (optimized) value. When the SV decreased by more than 30% below its optimized value, the VLS was repeated as dealt above.

In this institution the current standard fluid management in FFR surgery is described in the database containing data of patients who underwent FFR since 1999. The study group was compared with the matched historical control group. Matching characteristics were: demographics, ASA class, types of cancer, and free tissue flap, duration of surgery, necessity in tracheostomy, history of alcoholism, and preoperative hemoglobin.

Results of the study is preset in the table:

The duration of surgery, blood loss and urinary output were comparable in the study and control groups. The total volume of administered fluids, volume of crystalloids, and value of intra-operative positive fluid balance were significantly lower in the study group.

Conclusion: Continuous monitoring of stroke volume by the arterial waveform analysis and applying of the Stroke Volume Optimization Algorithm significantly decreased the total volume of fluid, and amount of crystalloids administered intra-operatively in patients undergoing Head and Neck Reconstructive Surgery.

This pilot study may serve as a foundation to a further randomized controlled study that will be conducted to determine the effects of the Stroke Volume Optimization Algorithm on the outcome in FFR patients.

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## THE EFFECT ON MYOCARDIAL INJURY BY ASPIRIN RESISTANCE IN PATIENTS AFTER OFF PUMP CABG

Lim T; Jeon Y; Bahk J

*Seoul National University Hospital*

**Background :** Although antiplatelet effects of aspirin are used to decrease ischemic complications of organs, mortality and graft thrombosis following off-pump CABG, aspirin resistance often occurs after off-pump CABG and can aggravate myocardial ischemic injury, graft failure and results in poor prognosis. Aim of this study is to quantitatively evaluate the adverse effect on myocardial injury by aspirin resistance after off-pump CABG.

**Methods :** We retrospectively studied 80 patients who underwent off-pump CABG, who received aspirin(100 mg) until the morning of the day of surgery. On the 1 day before operation, we tested blood samples for aspirin resistance by platelet drug response assay(VerifyNow™ Aspirin, unit : ARU). Aspirin resistance was defined as positive when the result was more than 550 ARU. Exclusion criteria were use of clopidogrel, emergency surgery, and off-pump CABG including any other operation.. According to the results, two groups were enrolled. one was the aspirin resistance negative group(ARN, < 550 ARU) and the other was the aspirin resistance positive group(ARP, > 550 ARU). Then we measured CK-MB, LD, and troponin I on 0, 1, 2, 3 and 5 day following operation. We also collected critical events; IABP insertion, VAD(ventricular assist device) placement, and myocardial infarction etc, which were occurred to patients during perioperative period.

Wilcoxon rank sum test was used to compare ARN with ARP for cardiac enzyme levels. One-way repeated measures of ANOVA was used to compare cardiac enzyme levels within groups. Fisher's exact test was used to compare groups for categorical variables. P value of < 0.05 was considered to be statistically significant.

**Results :** The results didn't show significant differences between ARN and ARP. But enzyme levels within groups were statistically significant( $p < 0.05$ ). There were no significant difference between two groups for occurrence of critical events.( $p < 0.05$ )

**Conclusions :** Although results were not significant, many papers suggested that aspirin resistance was related to cardiac enzyme elevation leading to myocardial injury. So if we control many confounding factors which were related to elevation of cardiac enzymes and increase sample size, we will be able to acquire more significant results.

**Reference :** Mangano DT. Aspirin and Mortality from coronary bypass surgery. N Engl J Med 2002;347:1309-17.

## THE EVALUATION OF POSTOPERATIVE OPHTHALMOLOGICAL COMPLICATION AFTER CARDIOVASCULAR SURGERY

Hayashi H; Kawaguchi M; Okamoto M; Hasuwa K; Matsuura T; Hara Y; Taniguchi S; Furuya H

*Nara Medical University*

**Introduction:** Postoperative ophthalmological dysfunctions following cardiovascular surgery are rare, but devastating complications, in part because it often produces severe visual loss and in part because once vision is lost, it rarely recovers. Reported causes of postoperative ophthalmological dysfunction include retinal artery occlusion, ischemic optic neuropathy or cerebral cortical visual impairment. Overall, the incidence range is reported between 0.06% in a retrospective review (1) and 25.6% in a prospective study that had ophthalmological screening examinations at a bedside (2). There are no prospective studies evaluated with ophthalmologically specialized examinations. We therefore designed a prospective study evaluating the incidence of postoperative ophthalmological complication after cardiovascular surgery with ophthalmologically specialized examinations.

**Methods:** After institutional approval and written informed consent were obtained, 51 patients undergoing elective cardiovascular surgery were enrolled in the study. All patients included 40 patients with cardiopulmonary bypass (CPB) and 11 patients without CPB. Anesthesia was maintained using a regimen of propofol or sevoflurane and fentanyl with neuromuscular blockade. All patients were assessed preoperatively and postoperatively with fundoscopy, measurements of visual acuity, intraocular pressure and critical flicker frequency, and examinations of visual field, eye movement and color abnormality by ophthalmologists. When new ophthalmological dysfunctions were found postoperatively, the postoperative findings were defined as abnormal.

**Results:** Permanent visual field deficits were observed in three patients with CPB, and the other ophthalmological examinations revealed no remarkable changes. Of the three, the postoperative new abnormal findings were asymptomatic central scotoma in a patient undergoing total arch replacement, symptomatic homonymous hemianopia in a patient undergoing total arch replacement and asymptomatic homonymous hemianopia in a patient undergoing Bentall operation. In contrast, patients without CPB had no postoperative new abnormal findings.

**Conclusion:** The present study indicated that the incidence of postoperative ophthalmological complication after cardiovascular surgery was 5.9% (3/51). Further study would be required for the etiology, effective treatment and prevention of postoperative ophthalmological complication after cardiovascular surgery.

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## THE FREQUENCY OF MEDICATION ERROR INCREASES BASED ON SURGICAL CASE TYPE

Cooper L; Digiovanni N; Taylor A; Schultz L; Nossaman B

*Ochsner Health System; University of Miami Miller School of Medicine*

**Intro:** Medication errors are a common occurrence in anesthesia (frequency of 1 out of every 130-200 anesthetics). Several factors may contribute to medication errors in anesthesia, including experience of the anesthesia provider and the complexity of the case (ASA classification). But can the type of surgical case contribute to medication errors? The aim of this study was to assess if certain types of surgical cases at a tertiary training hospital have higher frequency of medication errors than others.

**Methods:** Medication error reporting forms were designed and attached to every anesthetic record during a six month period (08/20/07-02/20/08). Anesthesia providers received training on what are considered medication errors before the start of the study. Providers were asked to voluntarily and anonymously return the reporting form for every anesthetic case whether or not a medication error occurred. If providers indicated positively (medication error occurred), further details of the medication error was requested, including type of surgical case. Type of surgical case for the negative response cases was obtained from the surgical informational system.

**Results:** Total 52 forms out of 10574 anesthetics were returned with a positive response, indicating a medication error/pre-error occurred. The incidence of medication error for each type of case was recorded and is shown in Table 1. As no errors were reported in Ophthalmology cases, all other case types were compared to this standard. Neurosurgery cases showed no significant increase from Ophthalmology, with an equal incidence of 0.00%. There were 5 errors reported in OB/GYN, resulting in an incidence of 0.31%. Although this may be clinically significant, there was no statistical significance. All other case types, including General, Orthopedic, ENT, CVT, Colorectal, Transplant (heart, liver, kidney, kidney/pancreas), and Peripheral Vascular, showed a statistically significant increase in error rate over the standard.

**Discussion:** CVT, colorectal, vascular, and transplant cases all were found to have an incidence of > 1.0%, resulting in a frequency of 1 in 66-100 anesthetics. These types of cases tended to include ASA III or higher, require multiple infusions, and typically required medications not frequently used in anesthesia. ENT cases were frequently pediatric cases, short in duration with fast turnaround, while most orthopedic cases were done with a regional technique, with or without a general, in older patients (hip replacements). Our findings show that a specific type of case has a higher incidence of medication error than previously reported. Previously reported error rates underestimate the true risk of medication errors in anesthesia due to statistical dilution from case types that rarely have errors. More complex cases on more complex patients lend themselves to increased rate of medication error.

## THE IMPACT OF INTRAOPERATIVE TRANSOESOPHAGEAL ECHOCARDIOGRAPHY ON CARDIAC SURGICAL PRACTICE

Klein A; Snell A; Nashef S; Hall R; Kneeshaw J; Arrowsmith J

### *Papworth Hospital*

The use of transesophageal echocardiography (TEE) during cardiac surgery has increased dramatically in the last 20 years and TEE is now widely accepted as a routine monitoring and diagnostic tool. We present the results of a prospective study to determine the relative contributions of unpredictable and predictable changes to the actual surgical procedure performed.

### Methods

The study population consisted of all patients undergoing cardiac surgery at Papworth Hospital between September 2004 and September 2007 in whom intraoperative TEE was performed. Changes to surgery resulting from TEE findings were subdivided into predictable (where TEE was planned specifically to guide surgery) and unpredictable (new pathology not diagnosed preoperatively).

### Results

Intraoperative TEE was performed in 2473 (44%) of 5591 cases. A change in the planned surgical procedure was documented in 312 (14.9%) cases. Of the 312 cases in which TEE led to a change in surgical procedure, 216 (69%) were predictable and 96 (31%) were unpredictable. The number of predictable changes to surgical management attributable to TEE increased significantly between 2004-5 and 2006-7 (8% versus 13%;  $p=0.025$ ). Of particular note, surgery was aborted in 5 patients after induction of anaesthesia and TEE examination.

### Discussion

Most changes to planned surgery as a result of TEE were due to the large number of cases where TEE was specifically requested to help determine the operative intervention, and where patients and surgeons agreed to defer the definitive choice of procedure until the time of operation. This has implications for consent and operative risk which have yet to be fully determined. The incidence of unpredictable change to the surgical procedure of was similar to that in other comparable series. It is possible that changes to surgical practice could become more frequent if all patients received intraoperative TEE. Such a policy would be difficult to justify based on current recommendations, and may lead to more complications.

## THE IMPACT OF RENAL RECOVERY ON SURVIVAL AFTER CARDIAC SURGERY-ASSOCIATED ACUTE KIDNEY INJURY

Hudson C; Phillips-Bute B; Shaw A; Stafford-Smith M; Cuthbert Hudson J; Patel U; Milano C; Swaminathan M

*Duke University*

**INTRODUCTION:** Postoperative acute kidney injury (AKI) is strongly associated with mortality after cardiac surgery. [1] However, it is unclear whether recovery of renal function confers a survival advantage. Therefore, we tested the hypothesis that in cardiac surgery patients, recovery of renal function after AKI is associated with improved long-term survival.

**METHODS:** Following IRB approval, we identified a cohort of patients who had isolated coronary bypass (CABG) surgery from 1996 to 2005 with postoperative AKI (peak postoperative creatinine (Cr) 50% greater than baseline within the first five days after surgery). Patients on perioperative dialysis and those who died within 10 days of surgery were excluded. Patients were followed postoperatively using standardized methodology. We assessed seven definitions of renal recovery in a series of multivariable logistic regression models with respect to their negative association with 1-year mortality. Each model was adjusted for baseline Cr, peak postoperative Cr, and Euro-score index. Internal validation was performed using bootstrap analysis. We examined the association of the most predictive renal recovery variable with long-term mortality using a Cox proportional hazards regression model. Survival curves were constructed using the Kaplan Meier method. A p-value of less than 0.05 was considered significant.

**RESULTS:** Incidence of AKI after CABG was 16%. Median follow up time was 40 months. The 1-year mortality in our cohort of 1310 AKI patients was 8.0% (n=91). Percent drop 24 (PD24 = percentage drop in Cr in the first 24 hours following peak Cr) was the single best variable negatively associated with one year mortality (or positively associated with survival) with a c-index of 0.724 and a bootstrap c-index of 0.729 (Table). Cox proportional hazards modeling showed a significant negative association between PD24 and long-term mortality. The hazard ratio for a unit change of 10 percentage points was 0.83 (95% confidence intervals 0.75-0.91) (Figure 1).

**DISCUSSION:** This is the first study to evaluate the role of renal recovery in patients who develop postoperative AKI. With PD24, we defined not only a statistically significant variable which is strongly associated with long term survival, but one that is relevant to clinical practice. Our findings emphasize the important role that renal recovery mechanisms may play in modifying the risk of mortality after AKI. Given the high mortality risk of AKI, measures that improve renal recovery may be among the most important interventions we make in improving outcomes after cardiac surgery.

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## THE INCIDENCE OF INTRAOPERATIVE AWARENESS IN CARDIAC SURGERY FAST-TRACK TREATMENT

Groesdonk H; Pietzner J; Koncar-Zeh J; Fassl J; Paarmann H; Mukherjee C; Ender J

*Heartcenter University Leipzig*

**Introduction:** Intraoperative awareness (i.e. recall), usually defined as explicit recall for intraoperative events, is an infrequent but well recognized adverse outcome after surgery under general anesthesia (1). This study was performed to investigate the incidence of intraoperative awareness with recall during this cardiac surgery fast-track treatment.

**Methods:** After institutional review board approval all patients (> 18 years) scheduled for cardiac surgery fast-track treatment during a 8-month period were entered into the study. Patients were excluded from the analyses if they could not complete the first interview within 24 hours postoperatively. All patients entered into this study were treated with our fast track concept(2). As part of the quality assurance program, each patient was interviewed by research staff with the same structured, modified Brice interview 3 within the first 24 hours. Follow up interviews were conducted at day 3 or 4 and day 6 or 7 after anesthesia, respectively. Awareness was defined by the presence of explicit memory of any event from induction of anesthesia to recovery of consciousness in the PACU.

**Results:** A total of 506 patients were interviewed. Ninety-seven percent (n=492) of the evaluable patients completed all three interviews, whereas all patients completed at least two interviews (we were unable to interview 14 patients (3 %) postoperatively at day 3 or 4 due to their postoperative confusion).

Nothing in the answers given by any of the patients in either of the three interviews indicated awareness, except for one 54 year old male patient. He responded positive to question no. 3 in the first interview and reported being awake for a short time and held down by someone, but felt no pain. After perusing the anesthesia and PACU chart, respectively, an open interview as performed by the first author to further elucidate this event the same day. Most likely this potential awareness took not place during the operation, but was due to an inadequate awaking at the PACU, which was treated by re-induction of anesthesia with a bolus of 50 mg of propofol. This event was detailed documented in the PACU chart. Because we cannot exclude that this patient was aware during the time of surgery, the incidence of awareness in this study is specified with 0,2 % (1 of 509 patients).

**Conclusion:** In conclusion, our institution has recently published the safety and effectiveness of the "Leipzig Fast-track concept", whereas the incidence of awareness has not been previously investigated. The incidence of awareness found in this prospective investigation is the lowest rate currently reported for fast-track cardiac anesthesia.

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## THE INCIDENCE OF POST-PNEUMONECTOMY ACUTE KIDNEY INJURY IS GREATER THAN/COMPARABLE TO AORTOCORONARY BYPASS SURGERY

Kushins S; Martin D; Phillips-Bute B; Stafford-Smith M; Onaitis M; Shaw A; Swaminathan M

*Duke University Medical Center*

**Background:** Acute kidney injury (AKI) is a common serious complication of cardiac surgery that is highly associated with mortality and morbidity (1). There is a perception that most non-cardiac surgical procedures (e.g., thoracotomy) are not associated with important acute kidney injury (2), although literature review suggests there is a paucity of data to support this opinion. We tested the hypothesis that postoperative AKI is more common after pneumonectomy than after coronary artery bypass grafting (CABG) surgery, and associated with poorer outcome.

**Methods:** With IRB approval, we gathered data for consecutive pneumonectomy procedures at a single institution between August 2001 and May 2008. Emergent surgeries and those involving extrapleural dissection or additional procedures (eg. large blood vessel reconstruction) were excluded. Data gathered included demographics, known renal risk factors (CHF, MI, PVD, DM, COPD, and HTN), epidural use, and perioperative variables (lowest hematocrit, transfusion). Postoperative AKI was defined using the AKIN criteria and as a linear variable using peak rise in serum creatinine as a percentage of baseline (% $\Delta$ Cr). Patients that died within 48 hours postoperatively were excluded (n=1). Poor outcome was defined as the composite of 30-day mortality, hospital stay more than 10 days or readmission within 30-days. This data was then compared to a previously described cohort of CABG surgery patients (1).

**Results:** Eighty-nine patients met inclusion criteria. Demographic variables were similar to those in other cohorts of thoracic surgery patients (2). AKI was common, occurring in 22/89 (24.7%) of patients. The 30-day mortality rate was 6.7%. The poor outcome composite occurred in 27 patients (30%) and was more common in AKI patients (59 vs. 21%; p=0.0007). Renal dysfunction (% $\Delta$ Cr) was also univariately associated with poor outcome (p=0.05). Compared to a previous sample of CABG surgery patients (1) % $\Delta$ Cr was higher (36.9 (47.7) vs. 22.1(36.3); p=0.003; figure 1). Multivariable linear regression analysis identified diabetes, advanced age, male gender, baseline creatinine and the absence of epidural analgesia as independent risk factors for increased % $\Delta$ Cr.

**Conclusions:** We found renal dysfunction after pneumonectomy to be more common than after CABG surgery, and highly associated with poor outcome. Predictors of post-pneumonectomy renal dysfunction are similar to those observed in other perioperative settings (1). These findings are relatively unappreciated in the management of post-pneumonectomy patients, and may be important in future studies to improve clinical care, including evaluation of epidural use and the often conservative intravenous fluid strategies employed in this population.

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## THE USE OF A NOVEL WARMING/COOLING CATHETER FOR COMPLEX CARDIAC SURGERY

Blitz A; Williams G; McFarland H; Okada S; Foster J

*University Hospital Case Medical Center; University Hospitals Case Medical Center*

Temperature management during the perioperative period can be a challenge for complex cardiac surgery. We herein report the use of a novel warming/cooling catheter for a clinical series of six patients.

The first 3 cases describe patients in whom the catheter was inserted intraoperatively so as to maintain and achieve perioperative normothermia. The first case is that of a 72-year-old male with severe COPD who underwent emergent repair of an aortic arch dissection requiring hypothermic circulatory arrest. The second case is that of a 58-year-old male with end-stage cardiomyopathy who underwent elective Heartmate LVAD insertion for Destination Therapy. The third case is that of a 78-year-old female who underwent salvage RVAD insertion for an acute right ventricular infarct with cardiogenic shock (see first temperature curve figure below).

The final 3 cases describe the use of the intravascular catheter as a tool for postoperative therapeutic hypothermia. The fourth case is that of a 56-year-old male who underwent urgent coronary bypass surgery and mitral valve repair, but suffered a full cardiac arrest after induction requiring cardiopulmonary resuscitation. In this patient, the intravascular catheter was used to cool the patient to 33 degrees for 48 hours after surgery to allow recovery from his perioperative stroke and seizures (see second temperature curve figure below). A fifth case is that of a 62-year-old male presenting with an acute Type A dissection and paralyzed, mottled lower extremities. The patient underwent dissection repair. After his perioperative bleeding subsided, the patient underwent cooling to 33 degrees for 48 hours in an attempt to minimize his spinal cord injury. As of 3 months postoperatively, the patient has been gradually recovering neurologic function of his lower extremities. The sixth case is that of a 74-year-old female with numerous comorbidities who underwent an uneventful CABG. On postoperative day 1, the patient suffered a dense focal stroke. She immediately underwent therapeutic hypothermia and recovered completely.

In all six cases, precise control of perioperative temperature allowed for a smooth perioperative recovery. No complications related to the intravascular catheter were noted. All six patients have survived and were discharged home. This clinical experience has paralleled results achieved in our porcine hypothermia model. Further studies are indicated to determine under which clinical circumstances this precise temperature management system would be of most benefit.

## THREE DIMENSIONAL PLANIMETRY OF MITRAL VALVE AREA FROM THE ATRIAL AND VENTRICULAR VIEWS AND COMPARISON WITH PRESSURE HALF TIME AFTER MITRAL VALVE REPAIR

Cummisford K; Mahmood F; Subramaniam B

*Beth Israel Deaconess Hospital; Beth Israel Deaconess Hospital*

### Introduction

The most accurate method of mitral valve area (MVA) measurement in the immediate post-cardiopulmonary bypass (CPB) period after mitral valve repair (MVR) with transesophageal echo is unknown. Pressure half-time (PHT) method is unreliable due to changing left ventricular (LV) compliance. Two-dimensional (2D) planimetry cannot be reliably used to trace the MVA, due to the non-planar shape of mitral annulus. We hypothesized three-dimensional (3D) echocardiography can be used to planimeter the mitral orifice immediately after MVR from the left atrial (LA) and LV perspective to calculate the "anatomical MVA" and will correlate with PHT.

### Methods

After IRB approval, data from patients who underwent elective MVR utilizing CPB was used for 3D MVA calculation. We used the Siemens Sequoia C512 ultrasound system (Mountainview, CA) with a V5M multi-plane TEE transducer equipped with the TomTec® (GmbH Germany) "On-Line Perspective Box". Five-degree cuts were obtained from the mid-esophageal position with R-wave gating from 0 to 180 degrees. The data sets were immediately exported into the "four-sight TEE" program for reconstruction and analysis using the following protocol to planimeter the MVA within the 3D data set:

1. In the four-sight TEE program, Tissue Threshold and Tissue Texture were used to optimize the appearance of the images.
2. Using the area demarcation tool, the mitral valve (MV) orifice was planimetered by tracing the margin of the mitral orifice from the LA and the LV perspective.

MVA was measured with the PHT method.

### Results

A total of 29 patients completed the study. The average time required for 3D data acquisition, reconstruction and MVA calculation was within 1-2 minutes in all patients. The mean 3D MVA measured from the atrial and ventricular views were 1.91 cm<sup>2</sup> (+/- 0.68 cm<sup>2</sup>) and 1.94 cm<sup>2</sup> (+/- 0.71 cm<sup>2</sup>) respectively and correlated well with a correlation coefficient of 0.977. The mean 3D MVA values and PHT did not correlate with a correlation coefficient of 0.006 and mean MVA of 1.93 cm<sup>2</sup> (+/- 0.71 cm<sup>2</sup>) and 3.09 cm<sup>2</sup> (+/- 0.79 cm<sup>2</sup>) respectively.

### Discussion

It was possible to calculate the MVA with planimetry in a 3D reconstruction of mitral valve within a few minutes of image acquisition. There was an excellent correlation between the 3D planimetered MVA's from the LA and LV perspective. There was no correlation between 3D and PHT MVA. PHT consistently overestimated the MVA when compared with 3D-planimetry. The unreliability of PHT for measuring MVA has been demonstrated in the past after mitral valvotomy [1]. 3D planimetry to measure the "anatomical MVA" may be method of choice to rule out mitral stenosis in the immediate post-CPB period due its lack of dependence on the loading conditions.

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## THREE-DIMENSIONAL GEOMETRIC ANALYSIS OF THE AORTIC VALVE

Karthik S; Mahmood F; Subramaniam B; Panzica P; Cummisford K

### *BIDMC*

The aortic valve apparatus consists of the left ventricular outflow tract (LVOT), aortic annulus, leaflets, sinuses of valsalva, sino-tubular (ST) junction and the proximal ascending aorta. We utilized a novel offline knowledge-based workflow algorithm software for automatic 3D reconstruction of the aortic valve apparatus available from Siemens ACUSON™ (Mountainview, CA). The software is able to dynamically assess the aortic valve apparatus geometry based on pattern recognition. This 3D reconstruction provides information about the dynamic changes in the dimensions of LVOT, annulus and ST junction as well as a continuous measurement of aortic valve area throughout the cardiac cycle (1).

### Methods:

After IRB approval, data was analyzed for five patients. 3D data sets were obtained using five-degree R-wave gated rotational acquisition of images. Mid-esophageal aortic valve images were obtained on a Siemens C512 Sequoia™ ultrasound system. The data sets were exported to an off-line computer and analyzed (Figure 1).

The data was analyzed with following protocol:

1. Image orientation: The aortic valve is oriented in a standardized plane.
2. Landmark Identification: The following anatomical landmarks are identified (Figure 1)
  - i. Aorto-Ventricular Junction (AVJ) – The junction of LVOT with the aortic valve annulus
  - ii. Aortic annulus
  - iii. Hinge Points (HP)- The junction of the mid-point of the base of the leaflet with the aortic annulus
  - iv. Leaflet tips (LT)
  - v. Sino-tubular junction (STJ)
  - vi. Sinuses of valsalva (SV)

### Results:

The software was able to analyze all the five data sets. The average time taken for analysis by the automated software was 1-2 minutes. The automated reconstruction required minimal manual correction. The software generated dynamic geometric models of aortic valve demonstrating the leaflet tip excursions, dynamic diameters of the LVOT, annulus, SV and the STJ (Figure 2). We were also able to analyze the aortic valve area over time during the cardiac cycle (Figure 2).

### Discussion:

It is possible to analyze the aortic valve geometrically utilizing 3D echocardiography. Contrary to the conventional 3D geometric assessment software programs, the aortic valve auto-analysis provides a dynamic geometric analysis through the entire cardiac cycle. This has the potential to improve our understanding of the mechanics of the aortic valve apparatus, particularly the aortic valve area.

Figure 1: 3D rendered image and analysis of the aortic valve apparatus

Figure 2: Area over time of the Aortic valve, AVJ, SV and the STJ

## TRANSESOPHAGEAL 3D ECHOCARDIOGRAPHY IS SUPERIOR TO 2D ECHOCARDIOGRAPHY FOR MEASURING LEFT VENTRICULAR OUTFLOW TRACT AREA

Andrawes M; Shook D; Novak T; Mitani A; Shernan S

*Brigham and Women's Hospital*

**Introduction:** Echocardiographic measurement of left ventricular outflow tract (LVOT) area is conventionally calculated assuming a circular shape and using a single diameter acquired from a two-dimensional (2D) transesophageal echocardiographic (TEE) plane. However, asymmetric LVOT geometry may result in inaccurate area measurements using 2D TEE techniques. Three-dimensional (3D) TEE permits acquisition of unique short-axis views of the LVOT, enabling direct planimetry of this area. We aimed to compare the accuracy of conventional 2D versus 3D TEE measurement of LVOT area and corresponding calculated cardiac output (CO), using thermodilution CO as a gold standard.

**Methods:** Full volume data sets of the LVOT were obtained and analyzed using a real-time 3D TEE matrix array (iE33; Q-LAB; Philips Health Care, Inc) in 9 cardiac surgical patients without significant valve regurgitation. The LVOT minor diameter (D1) was measured from a 2D TEE long-axis view created off-line by cropping the full volume 3D data set. A short-axis view of the LVOT was obtained from the full volume 3D data (Figure 1), enabling measurement of the major diameter (D2). LVOT area was determined by three methods: 1) assuming a circle and using D1 alone; 2) assuming an ellipse, using D1 and D2; and 3) direct planimetry of the 3D-acquired short-axis view. CO was calculated for each method by multiplying the corresponding LVOT area by pulse wave Doppler-acquired LVOT velocity time integral and heart rate. CO data was individually compared to the average of three consecutive thermodilution COs obtained during LVOT data acquisition.

**Results:** Mean LVOT area using D1 alone ( $3.15 \pm 0.41$  cm<sup>2</sup>) was significantly lower by 17% compared to using either D1 and D2 acquired from the 3D data set ( $3.78 \pm 0.48$  cm<sup>2</sup>;  $P < 0.0001$ ) or planimetry ( $3.78 \pm 0.47$  cm<sup>2</sup>;  $P < 0.0001$ ) (Table 1). There was no significant difference in LVOT area between the two 3D techniques. Similarly, the mean CO calculated using D1 alone was  $3.38 \pm 0.36$  L/min, a significant underestimation by 19% (95% CI 11-32%;  $P < 0.05$ ) compared to thermodilution. There were no significant differences in CO between the two 3D techniques or compared to thermodilution.

**Conclusion:** Conventional 2D TEE consistently underestimates LVOT area and corresponding calculated CO compared to two different 3D TEE methods, presumably due to unappreciated asymmetric LVOT geometry. 3D TEE permits acquisition of true short-axis views of the LVOT, enabling more accurate measurements of LVOT area and calculated CO.

## TRANSESOPHAGEAL 3-D ECHOCARDIOGRAPHY REVEALS SIGNIFICANT ASYMMETRIC GEOMETRY OF THE LEFT VENTRICULAR OUTFLOW TRACT

Novak T; Andrawes M; Shook D; Mitani A; Shernan S

*Brigham and Women's Hospital*

**Introduction:** Echocardiographic measurement of the left ventricular outflow tract (LVOT) area is conventionally calculated assuming a circular shape and using a single diameter acquired from a two-dimensional (2D) transesophageal echocardiographic (TEE) imaging plane. However, an asymmetric LVOT shape may result in inaccurate area measurements using 2D TEE techniques alone. We aimed to use three-dimensional (3D) TEE to demonstrate the progressive asymmetric ellipsoid geometry of the LVOT along its length.

**Methods:** Full-volume 3D data sets of the LVOT, which enabled unique short axis displays, were obtained and analyzed using a real-time 3D TEE matrix array transducer (iE33; Q-LAB; Philips Health Care, Inc.) in 8 cardiac surgical patients. The minor LVOT diameter and planimeted 3D areas were obtained by aligning the x,y, and z planes from full-volume 3D data sets. LVOT area was measured by 2 methods: 1) using the minor LVOT diameter and assuming a circular shape and 2) direct planimetry from the 3D acquired short axis view (Figure 1).

Measurements were made for each patient at 5 locations beginning just below the aortic valve annulus and at consecutive 0.25 cm intervals through 1.0 cm along the LVOT axis. Comparisons of LVOT area measurements by each technique were made at each level. The data were analyzed using a repeated measures ANOVA model with repeated subject effect.

**Results:** Mean LVOT area calculated from the minor diameter was significantly lower at each level compared to the 3D planimeted area (Figure 2). Furthermore, there was a trend toward an increasing difference in area measurements between the two methods at each level from the AV annulus through 1.0 cm below the annulus along the length of the LVOT.

**Conclusion:** LVOT area measurements obtained by assuming a circular shape and using a single diameter acquired from a 2D TEE plane may be significantly underestimated, and become progressively more inaccurate at distances farther away from the AV annulus along the LVOT length. Due to its asymmetric geometry, accurate LVOT area measurements should be made using 3D echocardiographic techniques.

Figure 1. Short axis displays of a typical LVOT acquired from full-volume 3D data sets. Images from a single patient acquired at 5 locations along the extent of the LVOT, showing differences in area measurements using the short axis diameter alone (D1) versus planimetry, beginning at the aortic valve annulus and at 4 consecutive 0.25 cm intervals through 1.0 cm.

Figure 2. Graphical and tabular representation of the LVOT area difference between 3D planimetry and D1 from the aortic annulus through 1.0 cm below the annulus.

## USE OF ON-Q® PAINBUSTER® IN MINIMALLY INVASIVE CARDIAC SURGERY DOES NOT REDUCE THE AMOUNT OF I.V. OPIOIDS POSTOPERATIVELY

Ender J; Fenske C; Mukherjee C; Wittmann M; Koncar-Zeh J; Banusch J; Groesdonk H

*Heartcenter University Leipzig*

**Introduction:** Pain therapy for cardiac surgery fast track patients is sometimes challenging. Therefore we investigated the effect of ON-Q® PainBuster® filled with ropivacain 0.375% on postoperative pain and the additional amount of opioids.

**Methods:** After approval of the local ethic committee and written informed consent 39 patients undergoing minimally invasive mitral valve repair using a left lateral minithoracotomy were included in this prospective, double blind clinical trial. At the end of the operation they were randomized either into verum or placebo group.. A On-Q-Soaker® catheter was placed after rib closure in the extrapleural space by the surgeon. The On-Q Pain Buster® system (Erda Medikal Pazarlama, Turkey) provided a continuous infusion of 5ml/h of either 0.375 % Ropivacain in verum group or 0,9 % sodium chloride in the placebo group over 72 hours. Additionally every patient got a PCA-pump with no continuous basal rate and a bolus of 2 mg piritramid. Severity of pain was measured daily using the visual analogue scale until the 5th postoperative day. Ropivacain blood concentration and  $\beta$ -1-acid glycoprotein level were measured 24, 48 and 72 hours after operation. Values are expressed as median with minimum and maximum.

**Results:** The amount of piritramid differed not significantly between both groups (see table 1). Only on the first postoperative day there was a significant lower pain score in the verum group (1.5) as compared to the placebo group (3) ( $p < 0.009$ ) (see table 2). Blood concentration of ropivacain in all patients were within the therapeutic range except for two times with concentrations of 4.1  $\mu$ g/ml.

**Conclusion:** The use of the ON-Q® PainBuster® did not provide significant pain release, except for the first postoperative day

## UTILITY OF THE TRANSESOPHAGEAL ECHOCARDIOGRAPHY SIMULATOR FOR RESIDENT TRAINING IN ECHOCARDIOGRAPHY

Panzica P; Bose R; Subramaniam B; Swaminathan K; Matyal R; Mahmood F

*BIDMC, Boston*

### Introduction:

Transesophageal echocardiography (TEE) is a valuable tool for evaluating anatomical and functional abnormalities of the heart and surrounding structures. The application of TEE as a monitoring modality is being recognized in non-cardiac surgery, consequently there is a pressing need for a comprehensive and efficient mode of training in echocardiography.

The prescribed curriculum mandates TEE training as a part of cardiovascular fellowship. Such opportunities are limited to major academic medical centers. With the exception of these, there are no organized training programs for physicians who are interested in "on the job echo training".

Furthermore, there is a significant "learning curve" associated with training in TEE. We utilized an innovative and state of the art "TEE simulator" to train anesthesia residents to perform comprehensive intraoperative TEE examinations in a simulated setting.

### Material and Methods:

We invited "echo naïve" anesthesia residents to participate in the simulator training. The TEE simulator from Heartworks London, UK was used for this purpose. Briefly, the simulator consists of a mannequin, a realistic TEE probe and a computer with high-definition monitor. An anatomically correct three-dimensional (3D) digital model of a beating heart is used for the purpose of simulation. The mannequin and the TEE probe are used to learn image acquisition. The TEE probe is attached with positioning sensors which translate the movements of the probe in relation to the digital beating heart. The scan plane can be rotated through the 3D digital heart to display the relevant anatomical cross sections and images, which appear as dynamic TEE acquired images.

The simulator has a whole variety of capabilities, most importantly the ability to simultaneously project echocardiographic and digital anatomical display (Figure 1). The simulator is also able to display intra-cardiac structures from multiple perspectives with annotated in-built text references.

Each participant performed five comprehensive exams under the supervision of an experienced echocardiographer.

### Observation:

All participants were able to perform a comprehensive TEE examination independently using the simulator. The participants were also able to visualize and correlate echocardiographic and digital anatomy. (Figure 1).

### Discussion:

The TEE simulator is a robust teaching and training tool to facilitate understanding of echocardiographic and functional cardiac anatomy along with echocardiographic image acquisition. Developing these skills is clearly one of the more challenging tasks early on in the training process. The simulator is conducive to learning at an individual pace without the time pressure and constraints of the operating room. It has the potential to enhance the quality of education and training in the operating room.

## WHAT IS THE BEST INDEX OF OXYGEN DELIVERY DURING CONGENITAL HEART SURGERY?

Tomita Y; Kurokawa S; Seino Y; Onuki E; Nomura M; Ozaki M

*Tokyo women's medical University*

### Backgrounds:

Maintaining adequate oxygen delivery is crucial for improving outcomes of congenital heart surgery patients.

Superior vena caval oxygen saturation (ScvO<sub>2</sub>), systemic arterial oxygen and superior vena caval oxygen saturation difference (Sa-vO<sub>2</sub>) and oxygen excess factor ( $\text{OEF} = \text{arterial oxygen saturation} / \text{Sa-vO}_2$ ) have been used to estimate oxygen delivery<sup>1</sup>.

The purpose of this study was to investigate the change of oxygen delivery during congenital heart surgery using a newly developed central venous oximetric catheter PediaSat™.

### Methods:

Twenty-six patients scheduled for congenital heart surgery enrolled in this study were further divided into two groups depending on preoperative arterial saturations as- cyanotic and non-cyanotic. We monitored continuous superior vena caval oxygen saturation (ScvO<sub>2</sub>) with PediaSat™ catheter and Vigileo™ monitoring system during surgery. SpO<sub>2</sub> and ScvO<sub>2</sub> were measured before incision and before and after sternal closure, and  $\text{OEF} = \text{SpO}_2 / (\text{SpO}_2 - \text{ScvO}_2)$  was calculated. In addition, blood lactate was measured after sternal closure. Statistical analysis was performed with the paired t, unpaired t and Mann Whitney U-tests. A p-value of < 0.05 was considered statistically significant. All values are shown as mean ± standard deviation.

### Results:

The range of patients age was 9 days – 8 years. 13 patients were non-cyanotic and 13 patients were cyanotic.

SpO<sub>2</sub> and ScvO<sub>2</sub> before incision were significantly higher in the non-cyanotic patients (99.5 ± 0.88% non-cyanotic vs. 83.2 ± 7.9% cyanotic, 81.6 ± 9.9 vs. 66.7 ± 9.6%, respectively).  $\text{OEF}$  before incision was higher in the non-cyanotic patients (7.3 ± 3.9 vs. 5.8 ± 3.0).

SpO<sub>2</sub> and ScvO<sub>2</sub> before and after sternal closure were similar (94.8 ± 7.4 vs. 95.6 ± 6.1%, 75.2 ± 13.2 vs. 74.4 ± 15.0%, respectively).  $\text{OEF}$  was decreased from 7.3 ± 6.6 to 6.5 ± 4.1 after sternal closure, but the change was not statistically significant.

SpO<sub>2</sub> and ScvO<sub>2</sub> after sternal closure were significantly higher in the non-cyanotic patients (99.3 ± 1.3 vs. 91.5 ± 6.5%, 79.4 ± 13.9 vs. 66.9 ± 15.9%, respectively).  $\text{OEF}$  was higher in the non-cyanotic patients (7.5 ± 5.0 vs. 5.1 ± 2.7).

The blood lactate levels were similar in both groups of the patients (2.8 ± 2.6 vs. 3.3 ± 2.5 mmol/L). There was no correlation between  $\text{OEF}$  and blood lactate level, between ScvO<sub>2</sub> and blood lactate level.

### Conclusions:

$\text{OEF}$  does not depend on the type of lesion compared to SpO<sub>2</sub> and ScvO<sub>2</sub>.

$\text{OEF}$  seems to be more sensitive to change of cardiac output than SpO<sub>2</sub> and ScvO<sub>2</sub>.

$\text{OEF}$  and ScvO<sub>2</sub> don't correlate with blood lactate level during surgical repair.

Continuous monitoring of ScvO<sub>2</sub> and calculating  $\text{OEF}$  may be useful for optimization of oxygen delivery in perioperative settings.

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