

A COMPARISON OF AKIN CREATININE RISE VS. AKIN OLIGURIA CRITERIA AS PREDICTORS OF LONG-TERM SURVIVAL IN POST-PNEUMONECTOMY PATIENTS

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

Duke University Medical Center; Gwinnett Medical Center, Lawrenceville, GA

Background: Acute kidney injury (AKI) is a serious and unfortunately common complication of cardiac surgery that is highly associated with decreased survival, both short- and long-term.(1,2) The Acute Kidney Injury Network (AKIN) has two diagnostic criteria for AKI — creatinine rise (≥ 0.3 mg/dL or 50% increase within 48hrs) or oliguria (<0.5 ml/kg/hr for >6 hrs). However, perioperative oliguria is a common finding, particularly when conservative intravenous fluid management strategies are employed (e.g., pneumonectomy surgery), and its relevance as a diagnostic criteria for AKI has come into question.(3) Therefore, we tested the hypothesis that post-pneumonectomy AKI as defined by creatinine rise is more strongly associated with decreased long-term survival than AKI as defined by oliguria.

Methods: With IRB approval, we gathered data from retrospective review of consecutive pneumonectomy procedures at a single institution between August 2001 and May 2008. Exclusions included emergent surgery and patients who died within 48 hours postoperatively (n=1). Postoperative AKI was diagnosed using the AKIN criteria for creatinine rise and oliguria, using daily serum creatinine values for the first ten days and hourly urine output for the first 48 hours postoperatively. Long-term survival was assessed using Social Security and National Death Indexes and hospital databases. If no date of death was found, survival was presumed. Long-term survival was compared for groups with and without AKI as defined by creatinine rise and oliguria.

Results: Eighty-eight patients met inclusion criteria and were followed for up to 2968 days (>8 years), with a median follow-up period of 700 days. Demographic variables were similar to those in other cohorts of thoracic surgery patients.(4) Association of long-term survival and acute kidney injury was assessed with Kaplan-Meier estimates. For AKI diagnosed by creatinine rise, the log-rank test showed a significant difference between the survival rates over time ($p=0.005$, Figure A). For AKI diagnosed by oliguria, log-rank tests showed no significant association ($p=0.86$, Figure B).

Conclusions: Acute kidney injury after pneumonectomy surgery as defined by AKIN creatinine rise criteria was strongly associated with decreased long-term survival in our study population, whereas there was no significant association of AKI with long-term survival as defined by AKIN oliguria criteria. Additional work is needed to confirm these findings with prospective studies; however, these findings question the validity of using oliguria as a clinical or research tool to diagnose AKI in the perioperative period.

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A METHOD FOR AUTOMATING 3D PISA CALCULATIONS

Rapo M; Hahm K; Gelfand B; McDonald J; D'Ambra M; Cobey F

Brigham and Women's Hospital; Daniel Webster College; Duke University and Brigham and Women's Hospital; M.I.T. (alumnus)

Background: The fundamental assumption underlying two-dimensional proximal isovelocity surface area (PISA) calculations is that the shape of the PISA is a hemisphere. In mitral stenosis (MS), this assumption is often not correct. Using Tomtec EchoView software, we demonstrate a novel method for assessing PISAs with non-hemispheric shapes and measuring the area of these irregular surfaces in three dimensions (3D). We also demonstrate the feasibility of automating 3D PISA calculation using a new code module we developed for Halcon HDevelop machine vision software.

Methods: After IRB approval, we evaluated 2D and 3D echocardiographic images of a patient with MS. Four separate PISA's were assessed which occurred sequentially during atrial contraction. The 2D PISA calculation based on a hemispheric model was used to estimate four corresponding orifice areas. Using TomTec EchoView software, 3D images of the PISAs, sequential 2 mm thick slices along a single axis were created. The boundary of each slice was manually traced using a quantitative ball and tracker which produced sequential arc lengths. (Image 1) Using individual arc lengths and distance between each arc, the surface area was calculated. The respective orifice areas were then determined. This manual approach served as a model for automating the process using Halcon HDevelop Machine vision software. For each arc, the contour of the boundary was automatically detected by separating the original image into red, green, and blue channels. The boundary shared by red and blue channels defined the contour of interest, distance was converted from pixels into millimeters, and a precise 3D surface area was generated and quantitative parameters determined, all automatically. This automated approach can make precise surface area measurements even if none of the semi-axes are equal or linear. 3D planimetry was used to calculate orifice areas for comparison.

Results: (see Image 2)

Conclusion: Orifice area (OA) changed as diastole progressed in MS, suggesting some flexibility of the leaflets. We developed a method to use machine vision algorithms for the calculation of 3D PISA. 3D PISA OA matched more closely with the three-dimensional planimetry values than did the OAs calculated in 2D, supporting the hypothesis that 3D PISA measurements may more accurately estimate valve OA. When calculating OA with PISA, one is actually calculating the slightly smaller vena contracta area. This may explain the difference between our planimetry values and the values calculated using PISA. Application of this methodology to a large series of patients will be the next step in assessing the value of this approach.

A RANDOMIZED, DOUBLE-BLINDED TRIAL COMPARING THE EFFICACY OF TRANEXAMIC ACID AND EPSILON-AMINOCAPROIC ACID IN REDUCING BLEEDING AND TRANSFUSION IN CARDIAC SURGERY

Rhee A; Shore-Lesserson L; Lazar D

Montefiore Medical Center; Mount Sinai Medical Center

Introduction: Prophylactic use of the synthetic antifibrinolytic agents epsilon-aminocaproic acid (EACA) and tranexamic acid (TA) have become the mainstay of blood conservation therapy since November 2007 when aprotinin was removed from the commercial market. The blood sparing properties of EACA and TA have been found to be adequate but inferior to those of aprotinin, but their side-effect profiles are assumed to be less serious. **Objective:** Our primary objective was to compare the effectiveness of EACA and TA in reducing bleeding and transfusion for on-pump cardiac surgery patients. We also sought to further examine the clinical benefits and adverse effects of EACA and TA. **Methods:** This is a single-center, randomized, double-blind comparison of patients undergoing cardiac surgery utilizing cardiopulmonary bypass (CPB), receiving EACA and TA in standard doses. Blood draws were obtained at three different time points to perform TEG, Rotem and D-dimer analyses. Primary endpoints were chest tube drainage and blood transfusions. Secondary endpoints 30 days after surgery include renal dysfunction, stroke, MI, death, cardiogenic shock, re-operation, and respiratory failure. Continuous data were analyzed using paired or unpaired Student t-test, as appropriate, or ANOVA for repeated measures. Data not normally distributed were analyzed with Mann Whitney-U test. Categorical data were analyzed using the Chi square test. We considered a $p < 0.05$ to be statistically significant. **Results:** This is an interim analysis of 81 patients studied, out of a total 196 projected to be needed by power analysis. There were no statistically significant differences between the EACA or TA in chest tube output at 12 and 24 hours. There was also no statistical difference in the intraoperative and 24 hour blood transfusion volumes, but a trend was present toward more transfusions in one group ($p < 0.1$). The number of patients receiving any transfusion trended toward a lower incidence in the group with lower transfusion volumes, but this also did not reach statistical significance (Chi square test, $p = 0.16$). Comparisons of baseline and 48 hour creatinine values were not statistically significant, nor was there a statistical difference between speed of clot formation and clot strength/firmness as measured by the Rotem and TEG. **Discussion:** Our data thus far shows that EACA or TA yield similar outcomes in chest tube output and the secondary outcomes that we sought to explore. There was a non-significant trend toward lower transfusion rates in one group, but we did not unblind ourselves for this interim analysis. There have been reports of seizure related to TA, which is also dosed by renal function, and is more expensive than EACA. Thus, if effectiveness is not superior using TA, this would be important to know. We will reevaluate our data at the protocol's completion and will continue to evaluate differences in bleeding-related and other adverse outcomes. **References:** 1. DA Fergusson et al. *N Engl J Med* 2008;358:2319-31. 2. PA Carless *BMC CV Dis* 2005, 5:19. 3. JH Levy et al. *Hematol Oncol Clin N Am* 2007;21:89-101 4. D Henry et al. *CMAJ* 2009;180:2.183-193.

ACUTE KIDNEY INJURY AND LONG-TERM SURVIVAL FOLLOWING PNEUMONECTOMY SURGERY

Meachem F; Randall K; Kushins S; Phillips-Bute B; Swaminathan M; Shaw A; Onaitis M; Stafford-Smith M

Duke University Medical Center; Gwinnett Medical Center

Background: Acute kidney injury (AKI) is a common serious complication of cardiac surgery that is associated with increased short and long-term morbidity and mortality.(1) Previously the incidence of renal injury following thoracic surgery was thought to be low and not associated with significant complications. However, we recently found that AKI is more common after pneumonectomy than coronary artery bypass surgery, and also associated with a more complicated postoperative course, including major adverse outcomes.(2) However, the relationship of post-pneumonectomy AKI with long-term survival has not been described. Therefore we tested the hypothesis that pneumonectomy surgery complicated by postoperative AKI is associated with poorer long-term survival.

Methods: With IRB approval, we gathered data for review for consecutive pneumonectomy patients at a single institution between August 2001 and May 2008. Excluded were those procedures involving extrapleural dissection or extensive vascular reconstruction, emergencies, and those that died within 48 hours (n=1). Postoperative AKI was defined using the AKIN criteria (a >50% postoperative increase in serum creatinine relative to the preoperative value) and also as a linear variable using peak rise in serum creatinine as a percentage of baseline (% \times creatinine). Survival data was obtained for all patients by chart review for hospital death summary or entries in the Social Security and/or National Death Indices. If no date of death was found, survival was presumed. Long-term survival was then compared between patients with and without AKI.

Results: Eighty-nine patients were followed up for as long as 2968 days (> 8 years), with a median follow-up period of 700 days. Association of long term survival and AKI was assessed with Kaplan-Meier estimates. The log-rank test showed significantly longer average survival for patients who did not sustain a perioperative acute kidney injury (Figure; p=0.005). Furthermore, a Cox proportional hazards regression analysis, including adjustments for age, weight, and gender found patients with AKI were 2.11 times more likely to die than those without AKI (95% CI for the hazard ratio =1.14-3.89, p=0.02 after adjustment).

Conclusions: In our retrospective study of pneumonectomy surgery, procedures complicated by postoperative AKI were a strong independent predictor for poorer long-term survival. These findings suggest that an emphasis on AKI avoidance and renoprotective strategies may contribute to improved survival after thoracic surgery. Prospective studies should be done to further explore this issue.

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ACUTE RV FAILURE WITH RIGHT-TO-LEFT SHUNT THROUGH PFO DURING LIVER TRANSPLANTATION.

Faraci J; Shillcutt S; Montzingo C

UNMC

A 51 year-old male with Hep C presented for liver transplantation. The patient's pre-transplant cardiac catheterization revealed: right dominant heart, 72% LVEF, normal wall motion, moderate AI, mild MR, and no significant CAD. TTE interpretation showed: mild AS, borderline LVH, borderline dilation of LA, trace TR, moderate AI, 60-65% LVEF and an intact interatrial septum with no evidence for an atrial septal defect. The preoperative TTE did not include documentation of a valsalva bubble study or the detection of a PFO.

Anesthesia performed an intra-operative TEE exam revealing a left-to-right shunting PFO; valsalva bubble study revealed reversal of the PFO shunt to a right-to-left shunt. After unclamping, TEE showed a large right atrial thrombus, increased right-sided pressures and PFO shunt reversal to a right-to-left shunt. RV function became severely compromised; the thrombus passed from RA to RV and then to the PA. Debris were seen to travel across the PFO into the LA due to a large increase in right-sided pressures. The patient briefly desaturated and had hemodynamic instability from RV strain. After the thrombus passed and right-sided pressures normalized, the patient hemodynamically recovered.

Reports of undiagnosed PFOs resulting in right-to-left shunts in organ transplant patients with normal pre-transplant cardiac evaluations are rare. Literature supports the use of TEE over TTE for detection of PFOs. Sensitivity of PFO detection in TEE vs. TTE is reported at 95% and 60% respectively.(9-12) 20-25% of the general population have undiagnosed PFOs, thus intra-operative TEE could drastically alter care in those patients.(1,2) Our case report shows an undiagnosed PFO, development of a right-to-left shunt and movement of thrombi. These sequelae can be diagnosed and managed by intra-operative TEE.(7-8) Shunt due to acute RV failure has disastrous cardiac, pulmonary, vascular and neurologic outcomes for the patient.(3) Debate exists as to early PFO closure benefits, but specific circumstances indicate improved surgical and clinical outcome potential.(4,5,6) Our institution performs over one hundred transplants per year, thus TEE plays vital role in our anesthetic management.

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ALGORITHMIC APPROACH TO REVERSING DECREASES IN CEREBRAL OXYGEN SATURATION IN COMPLEX CARDIAC SURGERY

Deschamps A; Denault A; Rochon A; Lebon J; Ayoub C; Qizilbash B; Couture P; Cogan J; Toledano K; Bélisle S; Hemmings G; Jean T; Blain R

Montreal Heart Institute, University of Montreal

Introduction: The risk for morbidity and mortality has been increasing for cardiac surgery. Because half of patients for cardiac surgery with cardiopulmonary bypass (CPB) will have some degree of post operative neurocognitive dysfunction(1), the brain should be a primary target organ for preventive strategies. Near-infrared reflectance spectroscopy (NIRS) is used as a non-invasive and continuous monitor of cerebral oxygen saturation (rSO₂). Using NIRS to reverse decreases in rSO₂ has resulted in shorter recovery room and hospital stay in non-cardiac surgery(2), and in a decrease in major organ dysfunction and in the length of stay in the intensive care unit after CABG surgery(3). NIRS monitoring remains controversial since baseline values are different between patients and no consensus exists on the kind or on the order in which interventions should be made to reverse decreases in rSO₂. An algorithmic approach to the correction of decreases in rSO₂ exists but this algorithm has not been tested in clinical situations. The purpose of this study was to test the efficacy of the algorithm in reversing decrease in rSO₂ in high-risk cardiac patients.

Methods: Institutional Ethics approval was obtained for this study. Prospective data was collected data from 209 consecutive high-risk patients scheduled for complex cardiac surgery. A significant decrease in rSO₂ was defined as a fall > 20% from baseline values for 1 min or longer. A successful intervention was defined as a return of rSO₂ above 20% baseline values. The number of interventions and the kind of interventions while following the algorithm were noted.

Results: Patients averaged 63 (range 20-87) years of age. Male:Female ration was 117:92. The most common surgeries included combined aortic valve replacement (AVR) and coronary artery bypass (30%), combined AVR and mitral valve replacement (15%), redo surgeries (8%), thoracic aortic aneurysm repair (8%), and congenital surgeries (5%). Baseline rSO₂ averaged 67 on the Left and 66 on the Right (L range: 15-95, R range: 15-95). A significant fall in rSO₂ values occurred in 48.8% of all patients and 40.2% of those had more than one decrease. These reductions occurred before CPB in 26.3% of cases, during CPB in 50.6% of cases and after CPB in 23.1 % of cases.

Algorithmic interventions were performed 165 times and 85.9% of interventions were successful. The algorithm was successful in increasing rSO₂ in 88.2% of the patients. The interventions used were as follows, increase of mean arterial pressure (31.8%), increase in end tidal carbon dioxide (18.8%), improving cardiac function or increasing CPB pump rate (12.5%), transfusion of blood (12.0%), head repositioning (5.7%), reposition of venous or arterial cannula (4.7%), deepening of anesthesia (2.3%), increase of inotropic agents (2.0%).

Discussion: Close to 50% of patients in high-risk cardiac surgery experienced a significant fall in rSO₂ values. Using an algorithmic intervention strategy resulted in the reversal of these decreases in close to 90% of cases. Whether successfully reversing decreases in rSO₂ values improves outcome in this patient population remains to be determined.

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ALTERED LEFT VENTRICULAR ROTATION IN A PORCINE MODEL OF ACUTE RIGHT VENTRICULAR PRESSURE OVERLOAD

Ho J; Chua J; Zhou W; Mackensen B; Mahajan A

Duke University; UCLA

BACKGROUND: While right ventricular (RV) dysfunction has been known to affect left ventricular (LV) stroke volume and function, the mechanisms for this mechanical dysfunction are not well elucidated. Preservation of normal rotational dynamics of the (LV) has been shown to be crucial to LV systolic and diastolic function. However, until recently, rotational dynamics of the heart have been difficult to quantify. Recent advances in ultrasound imaging and technology, including two dimensional speckle tracking, have enabled improved assessment of left ventricular function. We hypothesized that rotational dynamics of the LV are altered by RV dysfunction during acute RV pressure overload (RVPO), leading to decrease in cardiac performance. In this study we evaluated LV function using speckle tracking strain analysis to quantify the effect of RVPO on LV performance and twist mechanics.

METHODS: All animals received humane treatment in compliance with the 1996 National Research Council Guide for the Care and Use of Laboratory Animals and institutional approval. Seven anesthetized pigs (24 - 46 kg) underwent median sternotomy and placement of intraventricular pressure-volume conductance catheters. Epicardial echocardiographic images and LV pressure-volume (PV) loops were acquired for offline analysis at baseline and after banding of the pulmonary artery to achieve RV systolic pressures one half to one third of systemic pressure. PV data analysis included LV end systolic pressure volume relationships (ESPVR) and $+dP/dt_{max}$. 2-D echocardiographic images were analyzed for apical and basal twist (Figure 1), systolic twist rate (TR), Time to peak systolic twist (TTP), and apical peak untwist rate (UR).

RESULTS: RVPO resulted in decreased LV systolic twist at the apex relative to control (12.6 vs 8.9°) and reduced untwisting rate (-108 vs -69°/s). Systolic twist rate and time to peak twist were also reduced, while basal twist was not significantly altered. While a trend towards decreased ESPVR was not significant, LV $+dP/dt_{max}$, LVEDV, and cardiac output were reduced.

DISCUSSION: Ventricular interdependence causes a decrease in left ventricular function when the right ventricle experiences pressure overload. In this study, we demonstrate that RV dysfunction due to acute RV pressure overload alters LV rotational dynamics leading to a decrease in cardiac performance. Apical twist is the most affected rotational parameter; preservation of apical twist may be important in maintaining optimal LV performance.

ALTERED NEUROPEPTIDE Y1 RECEPTORS IN THE RIGHT ATRIUM OF TYPE II DIABETES MELLITUS PATIENTS

Matyal R; Mahmood, MD F; Bianchi C; Sellke F; Hess P

BIDMC

Introduction: Neuropeptide Y (NPY) is the most abundant long-acting neurotransmitter in the myocardium. It is involved in long-term structural changes after ischemia. NPY acts through multiple receptors especially neuropeptide receptor-Y1 (NPYR1). NPYR1 is involved in smooth muscle hypertrophy and calcium regulation. We hypothesized that there is altered expression of NPYR1 in the human myocardium of patients with type II diabetes mellitus causing diabetic cardiomyopathy.

Methods: After the Institutional Board Review approval the discarded right atrial tissue for cannulation from patients undergoing cardiopulmonary bypass procedure was collected. The tissue was used to determine NPYR1 by immuno-blotting and immunofluorescence.

Results: There were total 52 patients without diabetes and 25 patients with type II diabetes. The levels of NPYR1 were significantly higher in patients with type II diabetes mellitus as measured with Western Blotting ($p < 0.002$) (Figure 1). On immunofluorescence NPYR1 showed significant localization in the nuclei of the cardiomyocytes and the cytosol of vascular smooth muscle cells in atrial tissue of patients with diabetes mellitus as compared to patients without diabetes where it was localized in the endothelium.

Conclusion: Our study shows an up-regulation of NPYR1 in patients with diabetes mellitus. The predominant nuclear localization of NPYR1 may be involved in transcription of genes leading to myocardial hypertrophy and altered calcium regulation, thus causing diabetic cardiomyopathy.

ND: nondiabetic

DM: type II diabetes mellitus

$P = < 0.002$

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ANATOMIC CHANGES AFTER SURGERY FOR HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY:
SEPTUM, LVOT, MITRAL VALVE

HILLEL Z; SWISTEL D; BALARAM S; KULCSAR Z; KALAL K; SHERRID M

ST LUKES-ROOSEVELT HOSPITAL

INTRODUCTION. Hypertrophic obstructive cardiomyopathy (HOCM) involves obstruction of the left ventricular outflow tract (LVOT) by the anterior mitral valve leaflet (AML). HOCM is treated surgically when medical management fails to relieve symptoms to an acceptable degree. State of the art surgery involves 1. myectomy - partial thickness resection of the hypertrophic interventricular septum in the area of contact with the AML, 2. AML valvuloplasty - longitudinal or transverse plication, 3. papillary muscle release - incision to allow the antero-lateral papillary muscle to move posteriorly pulling the AML away from the LVOT. Routine use of intraoperative TEE in patients undergoing HOCM surgery had been recommended by cardiologists (Ref.1). We have investigated the changes in cardiac anatomy after surgical treatment of HOCM using intraoperative TEE.

METHODS. After informed consent for an institutional review board approved study, 24 patients undergoing surgical correction of HOCM were studied. Routine cardiac surgery monitoring was used and multiplane TEE performed with a Philips iE33 ultrasound scanner and a S7-2 probe. Routine moderate dose fentanyl cardiac anesthesia was administered without "fast-tracking". All data were collected before cardiopulmonary bypass (preCPB) and after stable weaning (postCPB) in a modified mid-esophageal 4-chamber view showing the LVOT at 0 rotation with one exception: the LVOT gradient was determined in the deep transgastric long-axis view using continuous-wave Doppler. Anatomic measurements performed off-line by one novice and one experienced echocardiographer were: interventricular septum (IVS) thickness, LVOT diameter, AML length, mitral annulus diameter (MAD), and distance from mitral annulus to mitral leaflet coaptation point.

RESULTS. No patient in our study group experienced ventricular septal defect complication. All patients showed a statistically significant reduction in LVOT gradient postCPB compared to pre. PreCPB IVS thickness was 2.36 CM compared to 1.84 CM postCPB ($p < 0.001$). LVOT diameter was 1.12 CM preCPB compared to 1.74 CM postCPB ($p < 0.001$). PreCPB AML length was 3.12 CM compared to 2.68 CM postCPB ($p = 0.05$). MAD was reduced but not significantly changed preCPB compared to postCPB (3.39 CM vs. 3.11 CM, $p = 0.14$). Annulus to coaptation point distance was unchanged (1.66 CM pre vs. 1.60 CM postCPB).

DISCUSSION. HOCM surgery causes significant changes in several but not all anatomic mitral valve parameters. TEE was useful in assessing the degree of the needed intervention before its application as well as its outcome. TEE demonstrated relief of the HOCM pathology in all patients. This study supports the routine use of TEE in HOCM surgery.

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[SPCHAR(deg)]

ANESTHETIC CONSIDERATIONS FOR PERCUTANEOUS AORTIC VALVE REPLACEMENT- INITIAL EXPERIENCE FROM SOUTH EAST ASIA

YUEN S; SUBRAMANI S

SINGAPORE GENERAL HOSPITAL

Background: Percutaneous Aortic Valve Replacement (PAVR) has been offered, on a compassionate basis, to patients with symptomatic aortic valve stenosis, with a life expectancy of more than a year and who is high risk for surgery(1). The procedure consists of two steps: an AV balloon valvuloplasty, followed by the deployment of a pericardial bioprosthesis mounted on a balloon-expandable stent. Rapid ventricular pacing is applied to deploy the bioprosthetic valve successfully, by suppressing left ventricular ejection. Imaging is provided by fluoroscopy and trans-esophageal echocardiography (TEE), which also used to assess the integrity of the valve. The native AV can be approached antegrade through the LV apex via a small thoracotomy or retrograde through percutaneous access via the femoral artery (2,3,4).

CLINICAL FEATURES: 7 patients underwent PAVR at our institution from February 2009 to June 2009. Patients' characteristics and outcomes are described in the table below. All 7 patients received the Edwards SAPIEN trans-catheter aortic valve and all were performed in the cardiology suite. 4 trans femoral (TF) and 3 trans apical (TA) procedures were carried out by a dedicated team comprising of cardiologists, cardiac surgeons, cardiac anesthesiologists and an experienced echo cardiologist. General anesthesia with a single lumen endotracheal intubation was employed along with standard cardiac invasive monitoring. Large bore intravenous access via an 8.5F sheath was inserted in all cases for rapid fluid administration if needed. A rapid volume infuser was available on standby at all times. A temporary trans-venous wire was inserted for pacing. At the end of the procedure patients were transferred to the cardiothoracic ICU for monitoring. 4 patients were extubated successfully in the cardiology suite and 1 patient was ventilated for 2 days in the ICU due to cardiac failure. One patient who underwent via TA was transferred to ICU and died after 4 hours due to cardiogenic shock secondary to acute myocardial infarction. Another patient who underwent via TF sustained iliac artery injury requiring open repair and CPR.

CONCLUSION: PAVR is a suitable alternative option in a group of patients not previously considered for surgery. One need to consider factors like previous sternotomy, previous chest wall radiation in addition to the standard EURO score for the patient selection. We would like to emphasis aortography in the end of procedure if via TF, to detect catheter related vascular injury. In addition we must always be vigilant and prepared for sudden hemodynamic instability which may be due to myocardial or vascular injury. Thorough knowledge in cardiac anesthesia and expertise in all technical aspects of the procedure is mandatory for successful outcome.

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ANTICOAGULATION MANAGEMENT DURING CARDIOPULMONARY BYPASS, A SURVEY OF 54 NORTH AMERICAN INSTITUTIONS

Lobato R; Carlson M; Shore-Lesserson L; Levy J; Despotis G; Bennett-Guerrero E

Barnes Jewish Hospital; Duke University; Emory University; GTC Biotherapeutics; Montefiore Medical Center

Background:

Despite an increasing number of evidence-based guidelines surrounding cardiac surgery[1], there remains a lack of standardization in the clinical management of anticoagulation during cardiopulmonary bypass (CPB). Further complicating the situation is a wide variability in patient responsiveness to heparin therapy. The purpose of the present analysis is to characterize the variability in anticoagulation management strategies for CPB.

Methods:

A survey questionnaire designed to investigate anticoagulation practice during cardiopulmonary bypass was sent to institutions in the United States (US) and Canada. Responses were collected and summary data were calculated for each question in the survey.

Results:

Responses were received from 54 sites (41 within the US; 13 within Canada). 78% of US respondents and all Canadian institutions in the survey used empiric weight-based dosing to guide initial heparin dose. The median initial empiric heparin dose was 300 IU/kg. 22% of US institutions used an in vitro heparin dose response method to determine the initial heparin dose. Minimum ACT required prior to instituting CPB ranged from <350 seconds to 500 seconds (Figure 1). However, the median value was 400 and 480 seconds, and 60-71% of institutions used a value between 400-480 seconds for Canadian and US centers, respectively. The maximum heparin dose administered to achieve target ACT prior to considering alternative therapies (e.g. plasma or antithrombin concentrate) is shown in Figure 2 with 54-77% of US and Canadian centers using a value over 500 IU/kg. Heparin resistance was treated almost exclusively with fresh frozen plasma (FFP) in Canadian institutions while US institutions employed either FFP or antithrombin concentrate.

Discussion:

The present results reveal marked variability in the management of heparin-based anticoagulation for cardiopulmonary bypass. Furthermore, substantial variation exists among different institutions with respect to diagnosis and management of heparin resistance. Possible limitations of survey studies include selection bias and non-response bias.

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ASSESSMENT OF SURGICAL SEPTAL MYECTOMY BY REAL TIME 3 DIMENSIONAL TEE

Lee M; Fischer G; Stelzer P; Varghese R

Mount Sinai Medical Center

Introduction: Hypertrophic cardiomyopathy (HCM) with dynamic left ventricular outflow tract obstruction (HCOM) was first described 50 years ago. Subaortic pressure gradients associated with this disease represent true impedance to LV outflow and are responsible for symptoms and mortality. Surgical myectomy can reduce these gradients and provide long-term survival benefit. We report the use of real-time 3-dimensional TEE imaging to assess the adequacy of surgical septal myectomy.

Case report: An 87 y/o female presented for aortic valve replacement, ascending aorta repair, septal myectomy, and coronary artery bypass surgery. Pre-cardiopulmonary bypass (CPB) TEE confirmed severe aortic stenosis (AVA 0.6 cm², transvalvular gradient 87 mmHg) and asymmetric septal hypertrophy (22 mm). Real time 3D images were obtained in the "live mode," and the narrowest area of the outflow tract was measured at end systole (0.61 cm²). (Image 2) The post-CPB TEE showed an enlargement of the LVOT diameter as seen by 3D TEE (Image 3) to 1.61 cm².

Discussion: Currently, evaluation of dynamic LVOT obstruction in patients with hypertrophic cardiomyopathy is performed using 2D echocardiography. If, as in the case we present, the patient has both dynamic LVOT obstruction and aortic stenosis the echocardiographer will be unable to use Doppler to quantitate either lesion, because the origin of the peak velocity is unknown. We confirmed the severity of aortic stenosis by planimetrically measuring the opening of the valve and assessed the degree of LVOT obstruction by measuring the narrowest area during end systole with integrated 3D software. Prior to resection, this gave us the ability to localize the precise area of obstruction. Post-resection, we were able to verify the adequacy of surgical resection by visualizing the patency of the entire LVOT in 3D prior to reversal of anticoagulation and removal of CPB cannulae. In conclusion, we report a case where the utility and superiority of using real time 3D echocardiography during surgical myectomy is clearly demonstrated. With the use of this technology, we would expect improved success of septal myectomy for dynamic LVOT obstruction.

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ASSOCIATION OF PERIOPERATIVE RISK FACTORS AND CUMULATIVE DURATION OF BISPECTRAL INDEX SUPPRESSION WITH LONG-TERM MORTALITY FOLLOWING CARDIAC SURGERY

Pal N; Kertai M; Palanca B; Searleman S; Zhang L; Burnside B; Finkel K; Avidan M

Washington University School of Medicine

Background: The association of preoperative risk indices with long-term mortality has previously been described for patients having cardiac surgery, but the relationships of intraoperative factors to mortality remain poorly defined. Current data suggest that mortality following non-cardiac surgery may be associated with persistent hypotension and the cumulative suppression of the processed EEG-based bispectral index (BIS). We sought to further characterize the perioperative factors associated with death following cardiac surgery and to determine the relationships between cumulative duration of BIS suppression (BIS<45), long-term mortality, and total anesthetic dose.

Methods: We studied 460 patients (mean age 63.0±13.1 years, 287 males) who underwent cardiac surgery between September 2005 and October 2006, at Washington University School of Medicine. Using multivariable Cox regression analysis, perioperative factors were evaluated for their potential association with long-term all-cause mortality.

Results: A total of 82 patients (17.8%) died during a median follow-up of 3 years (interquartile range, 2.7 to 3.3 years). Five perioperative factors were independently associated with increased mortality, namely Euroscore, red blood cell transfusion, cumulative duration of BIS suppression, intraoperative infusion of norepinephrine, and prolonged intensive care stay. Tranexamic acid administration and higher levels of preoperative hemoglobin were associated with decreased mortality. There was a weak inverse correlation between increasing end-tidal anesthetic gas concentrations during the anesthetic maintenance phase and BIS numbers for patients who died (Pearson's correlation coefficient [r]= -0.1992, red crosses, dotted regression line) and for those who survived (r = -0.2547, blue open circles; solid regression line) with no significant difference between the two correlation coefficients (p=0.71) [Figure]. Volatile anesthetic concentrations were not strongly associated with cumulative periods of BIS suppression. The 1.29 adjusted hazard ratio (95% CI, 1.12 to 1.49) for long-term mortality with cumulative duration of BIS suppression translated into a 29% increased risk of death for every cumulative hour spent with a BIS <45. The final multivariable Cox regression model showed a good discriminative ability (c-index of 0.78).

Conclusions: This study found an association between cumulative duration of BIS suppression and mortality in the setting of cardiac surgery. The weak association between cumulative duration of BIS suppression and volatile anesthetic concentration suggests that, beyond loss of responsiveness, the extent of processed electroencephalograph suppression may be more reflective of patient susceptibility than anesthetic dosing.

AUTONOMIC DYSFUNCTION AND RESPONSE TO SEDATION AND INDUCTION OF ANESTHESIA IN CARDIAC SURGERY PATIENTS

Deschamps A; Rochon A; Lebon J; Ayoub C; Qizilbash B; Couture P; Cogan J; Bélisle S; Toledano K; Pagé P; D'Antono B; Denault A

Montreal Heart Institute, University of Montreal

Introduction: Autonomic dysfunction is common in cardiac patients and can be measured by analysis of heart rate variability (HRV). Previous work has shown that >40% of cardiac surgery patients have autonomic dysfunction as measured by HRV and an abnormal response to the Valsalva maneuver (VAL)(1). Whether this dysfunction influences the patient's response to anesthesia for cardiac surgery is unknown. We therefore measured the autonomic response to sedation and to induction of anesthesia in cardiac surgery patients with and without autonomic dysfunction.

Methods: Informed consent was obtained for this study. Preoperative sedation consisted of 0.1mg/kg of subcutaneous morphine on the way to the operating room. Induction of anesthesia consisted of 1mcg/kg of sufentanil and 0.6mg/kg of rocuronium was used for endotracheal intubation. ECG and continuous BP was measured the day before surgery, with the patients sedated on the operating table for 5 min, during the induction of anesthesia, during intubation and for 10 min after intubation. The signals were saved on a portable computer for analysis of HRV and BP variability (BPV). The analysis of HRV and BPV was obtained using wavelet transformation.

Results: Sixty seven patients completed the study. Of those 38 (56.7%) had a normal VAL response and 29 (43.3%) had an abnormal one. Sedation resulted in an increase in HRV (parasympathetic tone) in the normal VAL group (18764.0 ± 3504.5 vs 35272.0 ± 6247.4 , $p < 0.001$) while HRV did not increase in the abnormal VAL group. Sedation resulted in a decrease in BPV (sympathetic tone) in both groups. With induction of anesthesia HRV decreased in the normal VAL group and this was followed by a sharp increase during intubation and a return to low values thereafter. In the abnormal VAL group HRV did not decrease at induction, did not increase with intubation but gradually decreased thereafter (Fig1). BPV decrease equally in both groups at induction and intubation. In the abnormal VAL group there was significant hypotension in the abnormal VAL group at induction (Fig2) and increased requirement for vasopressors to maintain BP at induction (Phenylephrine, 0.6 ± 0.3 vs 0.2 ± 0.1 mg, $p < 0.001$).

Discussion: Patients with autonomic dysfunction prior to cardiac surgery differ in their parasympathetic response to sedation, induction of anesthesia and intubation. These patients also have more hypotensive episodes during induction of anesthesia and that could put them at risk for perioperative complications. Increased baseline parasympathetic activity appears to be an important factor in autonomic dysfunction of cardiac surgery patients.

1-Abstract # 91012145139955-37

AXIS-ORIENTED VOLUME SCANNING TO FACILITATE ON-CART ANALYSIS OF REAL-TIME THREE-DIMENSIONAL TRANSESOPHAGEAL ECHOCARDIOGRAPHY

Seino Y; Yasuda T; Tajima K; Nomura M; Hirasaki Y

Tokyo Women's Medical University; Tsukuba Memorial Hospital

Background

Real-time three-dimensional transesophageal echocardiography (RT3DTEE, iE33, Philips Medical Systems) has been increasingly used in the setting of cardiac surgery [1]. RT3DTEE can display en-face images of the cardiac structures and also can provide very useful information that have an impact on surgical decision-making. However, handling of the 3DTEE dataset is complex. The orthogonal axes of each 3D image are set automatically according to the X-Y axes of the corresponding multiplane 2D TEE image (Figure 1). This feature makes on-cart analysis of the 3D datasets of limited value, because cropping along the axis (box cropping) of the 3D image does not necessarily provide clinically useful images. Arbitrary plane cropping is time-consuming and not reproducible. As a result, multiple 3D datasets that contain the same cardiac structures within a variety of orthogonal axes might be obtained in a single 3D TEE study, which might be considerably time-consuming and impose additional workload on the perioperative echocardiographer.

We therefore developed tips for RT3DTEE data acquisition that may facilitate on-cart analysis.

Method: Axis-oriented full-volume scanning.

1. Obtain a mid-esophageal mitral commissural (MC) view by the multiplane 2D mode.
2. Press "Full-volume" button, then the MC view and aortic valve long axis (AVLAX) view are displayed in the left and right views, respectively.
3. Adjust the scan area by turning the image priority knob to include the AV.
4. Try to adjust the position of the probe so that the left ventricular apex is aligned in the center of the sector.
5. Acquire full-volume data (MC full-volume).

The MC full-volume dataset can not only demonstrate 3D en-face images of the cardiac structures, but box cropping of the 3D image also allows visualization of many clinically useful slice images (Figure 2).

Discussion/conclusion

The strength of our present method is that a single 3D dataset can provide many useful images by simple on-cart manipulations; the assessment of the cardiac structures by RT3DTEE may, therefore, be facilitated.

Furthermore, standardizing the three-dimensional alignment of the heart in the dataset may allow the examiner to understand the image orientation easily.

In conclusion, the MC full-volume dataset seems to be useful for an efficient assessment of the cardiac structures using RT3DTEE.

The mitral commissure-commissure axis and AVLAX can be the key axes in three-dimensional assessment of the cardiac morphology. Further investigation is required to assess the feasibility of our method.

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BIOLOGICAL PATHWAY BASED ASSESSMENT OF THE HUMAN LEFT VENTRICULAR TRANSCRIPTOME RESPONSE TO ISCHEMIA DURING CARDIOPULMONARY BYPASS

Muehlschlegel J; Perry T; Gorham J; Sherman S; Aranki S; Seidman J; Body S

Brigham and Women's Hospital; Harvard Medical School

Introduction

Cardiopulmonary bypass (CPB) with cardioplegic arrest is associated with ventricular dysfunction mediated by metabolic substrate depletion, ischemia-reperfusion injury, apoptosis and necrosis. Whole-genome transcriptional profiling provides an unbiased examination of the regulatory pathways mediating responses to ischemia. We examined differential gene expression in left ventricular (LV) tissue samples from patients undergoing isolated aortic valve replacement (AVR) surgery with CPB prior to and after cardioplegic arrest.

Methods

Apical punch biopsies from the LV vent placement site were taken from patients undergoing AVR with CPB at two time points; immediately after aortic cross clamping (pre-ischemia), and immediately before removal of the aortic cross clamp (post-ischemia). Samples were placed in RNeasy lysis buffer (Qiagen, Inc.) for 48 hours prior to storage at -80C. The Illumina/Solexa Genome Analysis platform was used to quantify genome-wide mRNA expression using digital serial analysis of gene expression (DSAGE).

We used Ingenuity Pathway Analysis 7.6 (IPA; Ingenuity Systems) to identify fold change and significance values in differential gene expression during CPB between pre-ischemia and post-ischemia samples. Significant differences in gene expression were defined as a change in expression with a significance value $p < 0.01$.

Results

Median duration of aortic crossclamping was 81 minutes (range 80-94min). Tissue quality was high by electrophoresis (RNA integrity number >7.5 in all samples). IPA identified the top three canonical pathways as mitochondrial dysfunction ($P=3.6 \times 10^{-27}$), oxidative phosphorylation ($P=5.4 \times 10^{-27}$), and ubiquinone biosynthesis ($P=4.1 \times 10^{-12}$). The most highly up- and down- regulated genes represent cellular processes of energy production, cellular growth and proliferation, and cell death (Table 1). Intelectin 1, the most down-regulated gene with a mean 88.5-fold decrease in expression intensity across all patients, is involved in protein amino acid phosphorylation (Figure 1).

Discussion

The LV exhibits marked changes in gene expression profile in response to ischemia during CPB. Variations in these pathways represent important contributors to the pathophysiology of ventricular ischemia, and thus, may have serve potential as biomarkers of injury or therapeutic targets.

BLOOD TRANSFUSION IN THE POST-APROTININ ERA IN PEDIATRIC CARDIAC SURGERY

Mossad E; Teruya J; Fraser C; Reyes M

Texas Children's Hospital

Introduction: The serine protease inhibitor, Aprotinin has been removed from the US market since June 2008. The purpose of this report is to examine changes in bleeding risk and transfusion practices in children undergoing cardiac surgery on cardiopulmonary bypass (CPB) in the post-aprotinin era.

Methods: With IRB approval, we studied the anesthetic and transfusion records of patients <1 year old receiving Aprotinin (6/07-6/08) and compared the data to those of infants receiving amicar (6/08-6/09). Data collected including demographics, blood ordered, transfusion in the first 24 hours, and complications. Data was analysed using t-test for continuous variables and chi-square test for categorical variables. Data is presented as mean+/- SEM.

Results: There were 120 patients with Aprotinin and 89 patients with Amicar. The two groups were similar in age, weight, diagnosis (single ventricle repair), CPB and cross-clamp duration, redo operation and cooling temperature. The Amicar patients had a higher incidence of prematurity (Table I). There was no difference between the groups in chest tube drainage in first 24 hours, amount of blood transfusion needed, or the use of rFVIIa to control severe coagulopathy. However, the Aprotinin group had a lower platelet count postoperatively (0.08) and required more platelet transfusion ($p=0.02$). There was no difference in % change of serum creatinine between the group or in the number of required chest explorations for bleeding.

Conclusion: Although Aprotinin is a useful medication to control bleeding in children undergoing cardiac surgery, there was no impact for its absence on transfusion or bleeding in the population studied. Alternatives to aprotinin are as effective and devoid of its potential risks.

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BONE MARROW-DERIVED PROGENITOR CELLS AND ATHEROMA BURDEN IN CARDIAC SURGICAL PATIENTS

Bhatt H; Swaminathan M; Povsic T; Phillips-Bute B; Adams S; Zhou J; Peterson E; Mathew J; Milano C; Mackensen G

Duke University; Duke University Medical Center

Background: Endothelium is a major determinant of vascular homeostasis. Bone marrow-derived circulating progenitor cells (CPCs) proliferate and differentiate into mature endothelial cells and are important in vascular repair. Impairment in mobilization or depletion of CPCs is a marker for increased cardiovascular risk(1). While the association between CPC levels and cardiovascular risk has been shown, their relationship with aortic atheroma, an advanced form of atherosclerosis, is less clear. We therefore tested the hypothesis that the number of CPCs is independently associated with aortic atheroma burden.

Methods: With IRB approval and informed consent, blood samples were prospectively obtained preoperatively in 134 adult patients undergoing cardiac surgery without a history of ischemic insult within two weeks of surgery. Patients received a detailed assessment of aortic atheroma burden with transesophageal echocardiography. Samples were assessed for mononuclear cells (MNCs) positive for CD34/CD133 surface antigens by flow cytometry. CPC counts were log transformed to achieve a normal distribution. Atheroma burden was characterized using standard SCA/ASE guidelines. Atheroma quantification was validated offline by an independent observer blinded to CPC counts. The hypothesis was tested first using Spearman correlation between CPC counts and atheroma burden defined by maximal atheroma height or area. A multivariable linear regression model was developed with maximum atheroma height as the dependent variable and CPC count as the independent variable. Other covariables were age, weight, female gender, hypertension, diabetes, and tobacco use. All analyses were conducted on SAS (ver. 9.1.3, SAS Inc, Cary, NC). A p value of less than 0.05 was considered significant. With a sample size of 134, the study had 80% power to detect a correlation coefficient of 0.24 as significant.

Results: The median CPC counts at baseline were 3.8 cells/103 MNCs, while the average maximal atheroma height was 3.8 (range 1.8) mm. There was no correlation between CPC counts and either maximal atheroma height ($r=0.1$) or area ($r=0.05$). In the multivariable regression model, there was no significant association between CPC counts and maximal atheroma height ($p=0.49$). However, both tobacco use ($p=0.0003$) and age ($p < 0.0001$) showed a strong independent association with atheroma height.

Conclusion: We did not confirm our hypothesis that CPC levels are associated with aortic atheroma burden in cardiac surgery patients. While studies have reported an independent association between CPCs and cardiovascular risk, there is no consensus on the precise phenotype of progenitor cells that participate in vascular homeostasis (2). Moreover, cells may be functionally impaired which is not reflected by the number of circulating cells. Our study only investigated a quantitative relationship between CPCs and atherosclerotic disease and not functional ability of CPCs to protect against progression of atherosclerosis (3). Further studies are required to establish the mechanism and role of CPCs on atheroma burden in patients undergoing cardiac surgery.

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CARDIOPROTECTIVE EFFECT OF ELECTROACUPUNCTURE IN RABBITS WITH MYOCARDIAL ISCHEMIA AND REPERFUSION: INVOLVEMENT OF CARDIAC NOREPINEPHRINE RELEASE AND PROTEIN KINASE C SIGNALING

Mahajan A; Ho J; Zhou W; Patel S

UCLA

Background - Augmentation of cardiac sympathetic tone during myocardial ischemia has been shown to increase myocardial oxygen demand, arrhythmias, and infarct size in animal models. Our previous studies have demonstrated that electroacupuncture (EA) inhibits the visceral sympathoexcitatory cardiovascular reflex. The purpose of the present study was to determine the effects of EA on left ventricular (LV) mechanics, oxygen demand, arrhythmias, infarct size and in vivo cardiac norepinephrine release and its possible mechanisms in rabbits with myocardial ischemia and reperfusion (MIR).

Methods and Results - Anesthetized rabbits (n=22) underwent 60 min of left coronary artery (LCA) occlusion followed by 3 h of reperfusion. We evaluated the LV strain and twist by 2D speckle tracking imaging, ST segment elevation on electrocardiogram, ventricular arrhythmias, infarct size (expressed as a percentage of the area at risk), myocardial norepinephrine release by cardiac microdialysis and protein kinase C (PKC) signaling. The animals were subjected to the following groups: (1) untreated, no intervention either before or after LCA occlusion; (2) EA, Neiguan-Jianshi (P 5-6) acupoints were electrically stimulated at 2 Hz for 30 min immediately after the onset of LCA occlusion; (3) EA at nonacupoints; (4) EA plus chelerythrine (non-selective PKC inhibitor). MIR decreased the LV strain and twist while worsening ventricular arrhythmias, ST segment elevation, infarct size, myocardial oxygen demand and concentrations of myocardial norepinephrine. EA at P 5-6 significantly attenuated the deleterious effects of MIR, while EA at nonacupoints had no effects. However, the cardioprotective effects of EA were abrogated by pretreatment with Chelerythrine.

Conclusions - These data suggest that EA produces cardioprotective effects against MIR through an inhibition of cardiac sympathetic nervous system and PKC signaling mediates the EA action.

CHOICE OF COLLOID INFLUENCE POST OPERATIVE BLEEDING IN CARDIAC SURGERY.

Lebon J; Brouillette D; Verrette L; Nguyen A; Deschamps A; Couture P; Rochon A; Denault A; Denault A; Ayoub C; Qizilbash B; Toledano K; Cogan J

Montreal Heart Institute

INTRODUCTION Colloids are an important part of the fluid repletion strategy in cardiac surgery. However, there is limited comparative safety and efficacy data for the different colloid solutions available in cardiac surgery.

METHODS We conducted a prospective, unblinded, observational study comparing Pentaspan® (250/0.45/10%) and Voluven® (130/0.4/6%). Colloids were alternated each month for 6 months in adult patients undergoing cardiac surgery in our institution. Data was collected on colloid exposure (volume), renal safety (acute kidney injury and renal replacement therapy) and bleeding (volume of blood loss and transfusion exposure).

RESULTS 626 patient files were reviewed. There were no statistically significant differences in patient demographics and surgical characteristics. The preoperative risk assessment for bleeding and renal failure was similar in both groups. Volume required to maintain hemodynamic stability was higher for Voluven® (3583 vs 3357 ml, $p=0.0065$). There was no observable difference in acute kidney injury or the need for post-operative renal replacement therapy between the two groups (Figure 1). Post-operative blood loss was statistically lower for Voluven® (757 vs 900 ml, $p=0.0275$) (Figure 2). The difference in bleeding was more important in patients younger than 60 years old (663 vs 1000 ml, $p=0.0137$) and in patients scheduled for elective surgery with a cardio pulmonary bypass (CPB) shorter than 60 minutes (720 vs 910 ml, $p=0.0064$) (Figure 3). Although patients in the Pentaspan® group bled significantly more in the post-operative period, there were no difference in transfusion exposure.

CONCLUSION The choice of colloid solution can influence post operative bleeding in cardiac surgery. Voluven® is associated with less post-operative blood loss, particularly in younger patients with a shorter CPB. Transfusion exposure was similar in the two groups. A larger study will be needed to assess if this product can promote blood conservation in this specific population where we wish to actively restrict blood product use.

CLEVIDIPINE + PROPOFOL IN CARDIAC SURGICAL PATIENTS: LIPID LOADING OR HYPERALIMENTATION?

Klopman M; Cabalza J; Ziegler T; Paciullo C; Levy J

Emory University Hospital; Emory University School of Medicine

Background: Clevidipine is a novel short-acting intravenous agent used to treat acute hypertension. Cardiac surgical patients often receive high doses of propofol and/or clevidipine that are both formulated with soybean oil-based lipid emulsion (Intralipid[SPCHAR(reg)], Baxter Healthcare). Clevidipine is mixed in 20% Intralipid[SPCHAR(reg)] while propofol is mixed in 10% Intralipid[SPCHAR(reg)]. The clevidipine package insert (PI) lists the maximal daily dosage as 1000 mL (an average rate of 21mg/hr (42mL/hr) because of "lipid load restrictions."⁽¹⁾ While patients typically do not receive more than the recommended daily dose of clevidipine or the extrapolated maximum daily dose of propofol, the combined lipid emulsion load from both drugs has not yet been examined. Therefore, we evaluated lipid emulsion administration when both drugs were used in cardiac surgical patients.

Methods: After IRB approval, we collected the total time of and volume of propofol and clevidipine administered in 36 ICU patients, and calculated the total lipid emulsion administration. We report the total lipid load, total calories, and averages of these on a per-kilogram per-day basis.

Results: (table 1)

Discussion: The maximum daily lipid emulsion dose as defined by the PI of clevidipine and Intralipid[SPCHAR(reg)] was not exceeded in our patients. The PI for 20% Intralipid[SPCHAR(reg)] states "the daily dosage should not exceed 2.5 g fat/kg of body weight."⁽²⁾ Based on this, an 80-kg patient should not receive more than 1000 mL/d. While the propofol PI does not list a maximum daily dose⁽³⁾, it is easily calculated to be 2000 mL/d (83mL/hr) using the 10% intralipid PI. Recently published guidelines for parenteral nutrition recommend a lower maximal dose of lipid emulsion of 1.0-1.3 g/kg/d; equivalent to a daily maximum of 520 mL/d of clevidipine or 1040 mL/d of propofol⁽⁴⁾. Using these guidelines, one of our patients received >1.3 g/kg/d (table 1). Rare cases of significant parenteral lipid overdosage ("fat-overload syndrome") include hepatosplenomegaly, increased levels of serum transaminases, leukocytosis, coagulopathy, fever, hypoxia, and shock. One patient had a seizure that was unrelated to lipid infusion, as the lipid load was only 0.1 g/kg/d. No other adverse effects of lipids were noted. We therefore conclude that under normal clinical use in our series, there was no evidence of lipid overload in patients receiving clevidipine and/or propofol.

As shown in Table 1, patients received a mean lipid emulsion dose from these drugs of 5.9 kcal/kg/d, or ~25% of typical daily adult energy requirements in the ICU⁽⁴⁾. This important source of energy should be considered in daily orders for lipid emulsion in parenteral nutrition.

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CLEVIDIPINE IN A CARDIAC SURGICAL ICU: EXTENDED CLINICAL USE

Klopman M; Cabalza J; Paciullo C; Zellinger M; Levy J

Emory University School of Medicine

Introduction: Clevidipine is a novel, ultra short-acting intravenous (IV) dihydropyridine calcium channel blocker and a selective arteriolar vasodilator used for hypertensive urgencies and/or emergencies. In clinical trials, clevidipine was well tolerated for <72 hours, however most reported data is limited to ~5 hours (1). In clinical practice, prolonged infusions are often required in intensive care unit (ICU) settings. Therefore, we examined its use in cardiac surgical ICU patients.

Methods: Following institutional approval, all ICU patients (n=36) receiving clevidipine were evaluated over a 6-month period. Data collected included: clevidipine duration, volume, dose, blood pressure (BP) maximum (max) and minimum (min), and ICU length of stay (LOS) (see Table 1). Patients were rapidly weaned off of IV clevidipine as soon as possible by restarting preoperative antihypertensives, beta-blockers or amlodipine. Further, if patients were receiving higher doses of clevidipine to control BP, then IV beta-blockers (metoprolol or labetalol) were administered if the patient was tachycardic or to control heart rate.

{Table 1}

Results: Results are noted in table 1. We noted clevidipine was administered for a mean of 24 (range: 2-133) hours. Volumes infused never exceeded the recommended daily dosing of 1000 ml. This was due to attempts to minimize IV use and facilitate transition to oral medications as soon as possible. There were no adverse events noted in the clevidipine treated patients.

Conclusions: Clevidipine was well tolerated with no overshoot reported in our patients. There was one systolic BP measurement of 66 mmHg noted during a seizure thought to be related to tranexamic acid. Rapid conversion to oral therapy or adjunctive beta-blocker use was important in weaning IV use. Further data is necessary to evaluate long-term clevidipine use in patients.

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COMPARATIVE ANALYSIS OF THE ENDOTRACHEAL CARDIAC OUTPUT MONITOR (ECOM) TO THERMODILUTION IN CARDIAC SURGERY PATIENTS

Ball T; Patel V; Culp B; Song J; Gloyna D; Ciceri D; Culp, Jr. W

The Texas A&M University System Health Sciences Center; The Texas A&M University System Health Sciences Center College of Medicine, Scott & White Memorial Hospital

BACKGROUND: Thermodilution (TD) using the Swan-Ganz catheter remains the gold standard for measuring cardiac output (CO). However, its small but inherent risk has prompted a search for a minimally invasive alternative for monitoring CO. The endotracheal cardiac output monitor (ECOM), a new FDA-approved device can provide CO measurements via an endotracheal tube and has the potential to be such an alternative. ECOM uses three-dimensional bioimpedance from a specially designed endotracheal tube in conjunction with an arterial line. The endotracheal tube contains seven silver electrodes on the cuff and tube which continuously measure the bioimpedance signal from the ascending aorta, which after processing, provides continuous CO, stroke volume, cardiac index, and systemic vascular resistance values. The software and array automatically compensate for variations in patient respirations, heart rate, patient position and tube position. ECOM has yet to be fully validated in the perioperative setting. We present a pilot study comparing ECOM with simultaneous TD CO. **METHODS:** After obtaining institutional review board approval, 40 unselected patients undergoing cardiac surgery were enrolled. Simultaneous comparative data points were collected from ECOM and TD in four operative periods: post induction, post sternotomy, post cardiopulmonary bypass, and post chest closure. Serial CO measurements were performed via TD until three measurements within 15% of each other were obtained which were then averaged and recorded as the mean TD CO for that period. The mean TD and ECOM data within each collection time period were then assessed for agreement with Bland – Altman, linear regression analysis, and percent error as described by Critchley and Critchley (1,2,3) when comparing a novel CO device to TD. **RESULTS:** The study population included 35 (87.5%) men with a mean age of 66 (\pm 10.7) years. When comparing COECOM to COTD for each time period separately, the Pearson correlation coefficients (*r*) were 0.50, 0.33, 0.42, and 0.48 for post induction, post sternotomy, post CPB, and post chest closure respectively. Bias and 95% limits of agreement in L/min. were -0.11 (-2.40 to 2.18), 0.04 (-2.57 to 2.65), -0.06 (-2.86 to 2.74), and 0.02 (-2.42 to 2.45) respectively. Percent errors were 51%, 53%, 50%, and 47% respectively. The overall combined mean CO was 5.05 L/min. No complications from the device were noted. **DISCUSSION:** Due to the intrinsic error associated with the pulmonary artery catheter, the acceptable limits of agreement for TD when compared to invasive reference methods are \pm 1.5 L/min. In our study, ECOM bioimpedance measurements of CO do not fall within these acceptable limits when compared to TD, nor do they fall within the acceptable percent error of \pm 30%. These results are similar to those reported for other bioimpedance devices for measuring CO when compared to TD (1,2). ECOM does not adequately agree with TD in patients undergoing cardiac surgery.

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CU2010, A NOVEL SERINE PROTEASE INHIBITOR WITH POTENT ANTICOAGULATION EFFECTS.

Szlam F; Tanaka K; van de Locht A; Dietrich W; Levy J

Emory University; Institute for Research in Cardiac Anesthesia; The Medicines Company

Introduction: CU2010 is a novel synthetic inhibitor of multiple serine proteases including factor Xa and plasmin (1). Because antifibrinolytic therapy is routinely used in cardiac surgery, it is important to evaluate its effects with other hemostatic agents, or for its prothrombotic potential. Therefore, we evaluated the combined effects of CU2010 and recombinant factor VIIa (rFVIIa) on thrombin generation (2).

Methods: CU2010 and rFVIIa were obtained respectively from the Medicines Company (Leipzig, Germany) and NovoNordisk (Bagsbaerd, Denmark). CU2010 was added to stored platelet-poor plasma samples, collected from 5 consented healthy volunteers, at final concentrations of 0, 0.25, 0.5 and 1 μ M, and thrombin generation was measured using 2 pM tissue factor as a trigger. To some plasma samples, rFVIIa was added at a clinical concentration of (60 nM). The following parameters of thrombin generation assay were compared between samples: calculated initial rate of thrombin generation (peak thrombin/time to peak - lag time) expressed in nM/min and peak thrombin (nM). Lag time of thrombin generation was defined as the time from the addition of reagents until first burst of thrombin. Additionally, the effect of CU2010 (0-10 μ M) on inhibition of factor Xa was also evaluated at 37°C using human factor Xa (0.58 μ M) and Z-Gly-Gly-Arg-AMC (Diagnostica Stago, Parsippany, NJ) as FXa substrate. The progress of reaction was monitored (increase in fluorescent signal) using microplate format and Flex Station II system (Molecular Devices, Sunnyvale, CA).

Results: CU2010 decreased the rate and peak of thrombin generation in a concentration dependent manner (fig 1). The rate of thrombin generation was decreased maximally by $61.8 \pm 5.1\%$ and the peak by $40.8 \pm 8.5\%$ at 1 μ M concentration of CU2010; nevertheless the peak remained above 150 nM (hemostatic level). Increased rate of thrombin generation with rFVIIa was also reduced in the presence of CU2010 (fig 1). CU2010 dose dependently inhibited factor Xa (decrease in V_{max}/sec , fig 2).

Conclusions: The present data support the potent anticoagulation effect of CU2010, and demonstrate that increased FX activation induced by exogenous rFVIIa can be reduced by anti-Xa activity of CU2010. Because antifibrinolytic therapy has been associated with systemic thrombosis (3), the combined anti-Xa property of CU2010 may be favorable to mitigate a prothrombotic effect as demonstrated by rFVIIa in our model, or associated with CPB when antithrombin is depleted.

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CURRICULUM MANAGEMENT AND ASYNCHRONOUS COMMUNICATION IN GRADUATE MEDICAL EDUCATION: MODELING A CLINICAL FELLOWSHIP

Haddy S

Keck School of Medicine, University of Southern California

Background

Because graduate medical education has traditionally been “apprenticeship based” curriculum management tools have been slow to gain acceptance. As duty-hour restrictions decrease patient contact opportunities, chance encounters no longer guarantee a complete educational experience (1) and curricula are becoming more formalized. We modeled an Adult Cardiothoracic Anesthesia Fellowship curriculum as a “course” using an available curriculum management tool (Blackboard™).

Method

The course is divided into: Core Operating Room, Intensive Care Unit, and Transesophageal Echocardiography sections, each with its own syllabus. The course outline was taken from the Program Requirements for Adult Cardiothoracic Anesthesiology. (2) “Adaptive release” of the course content allows the instructor to stipulate the order of study or otherwise control the flow of content to the learner based upon performance criteria. Extensive monitoring capabilities allow the instructor to follow the progress of each learner. Learning resources are divided into some of the broad categories of tools in the ACGME Toolbox (3). The “Journal” is used to create a case-log, which is a personal reflective tool promoting Practice Based Learning and Improvement and evaluates medical knowledge, professional teaching, information technology, communication, and other required competencies. Faculty review the journal, comment, and add learning content in various forms. The “Discussion Board” is used by the trainees and faculty to discuss interesting cases or topics and as a “virtual journal club”. Asynchronous teaching and communication is proving increasingly valuable as trainees spread across several venues, and “float” or “night shift” rotations (necessary to comply with duty hour restrictions) make formal rounds and lectures difficult to schedule.

Discussion

The “course” in cardiothoracic anesthesiology is in development, but responses to demonstrations have been favorable. Faculty support is key, and not always easy to obtain. (4) Personnel with expertise in management of CMS environments are critical (4, 5) to help physicians bridge the gap between the course content, and a final product suitable for distribution within a CMS. (6) Once the “content” is properly developed (digitalized in a standardized format, i.e.: as “reusable learning objects”), its manipulation and distribution become possible in ways that dramatically expand its potential and value. These possibilities, which include sharing of modules among programs, could lead to standardization of curricula.

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DELIRIUM AND COGNITIVE DYSFUNCTION AMONG THE ELDERLY AFTER CARDIAC SURGERY: A COMPARISON OF CORONARY ARTERY BYPASS GRAFTING AND VALVE SURGERY

Nonaka T; Baba T; Fujimoto M; Otomo S; Maekawa K

Kumamoto Chuo Hospital

OBJECTIVE: Valve surgery has carried a higher risk of neurological dysfunction than coronary artery bypass grafting (CABG). This is due mainly to embolization from the surgical field during intracardiac surgery. However, the risk neurologic damage is increasing in patients who undergo CABG because the procedure is being performed more often on older patients with systemic atherosclerosis. The purpose of this study was to determine the incidence and etiology of postoperative delirium (PD) and cognitive dysfunction (POCD) after cardiac surgery in elderly patients.

METHODS: Data were collected prospectively on 247 patients (>60 years) who underwent elective valve surgery (VS group, n=152) or on-pump CABG (CABG group, n=95) between October 2004 and September 2009. All patients had preoperative magnetic resonance imaging (MRI) and angiography to assess prior cerebral infarcts and craniocervical artery stenosis. Carotid and epiaortic ultrasound were performed at the time of surgery to assess atherosclerosis of the carotid artery and ascending aorta. Four cognitive tests were performed preoperatively and 1 week postoperatively. Cognitive dysfunction was defined as a decrease of at least 20% from baseline for an individual's performance in more than two tests. Delirium was assessed by the Delirium Rating Scale, performed postoperatively daily for 3 days after extubation. We defined delirium as scores above 12 on the DRS. We compared the incidence of stroke, PD, POCD, risk factors and systemic atherosclerosis between the VS and CABG groups.

RESULTS: Two CABG patients suffered strokes but none of the VS patients (P=0.07). PD and POCD occurred respectively in 16 (6.5%) and 42 patients (17.0%), 9 patients developed both conditions. CABG patients were younger (71.3±6.6 vs 73.3±6.3 y.o.) and had a lower incidence of atrial fibrillation (3 vs 30%), but were more likely to have diabetes mellitus (44 vs 20%), hyperlipidemia (60 vs 26%), to smoke (57 vs 34%), aortic atherosclerosis (16 vs 6%), and carotid artery stenosis (15 vs 2%) than VS patients (P<0.05). The incidences of PD and POCD were higher in the CABG than in VS group (PD; 10.5% vs 3.9%, POCD; 24.2% vs 12.5%, P<0.05). Additionally, being male, having cerebral vascular disease and preoperative cognitive impairment (Hasegawa Dementia Scale<24) were risk factors only of PD. Peripheral vascular disease, cerebral infarcts on MRI and high plaque scores of carotid arteries were risk factors for both PD and POCD

DISCUSSION: Our results suggest that elderly patients who undergo CABG have a higher risk of PD and POCD that may be attributed primarily to systemic atherosclerosis. Although similar etiologies may underlie both PD and POCD, further study is needed to investigate the association between PD and POCD.

CONCLUSION: Elderly patients with systemic atherosclerosis who undergo on-pump CABG are at greater risk for PD and POCD compared to those who have valve surgery.

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DEPLETION OF S-NITROSYLATED HEMOGLOBIN IN AUTOLOGOUS WHOLE BLOOD

Caswell J; Hill S; McMahon T; Zhu H; Stamler J

Duke University

Background: Recent studies have questioned the risk/benefit ratio for red blood cell (RBC) transfusion. Despite the ability of RBCs to carry oxygen, improving the hematocrit does not always improve tissue oxygen delivery and transfusion of RBC's can be associated with ischemic events.[1] The disconnect between oxygen content of blood and tissue oxygen delivery reflects the fact that capillary blood flow is a major determinant of tissue oxygen delivery. [2] RBC hemoglobin (Hb) releases the vasodilator nitric oxide (NO) as a function of hypoxia, thus matching O₂ delivery with tissue demand by regulating microvascular blood flow. Depletion of S-nitrosylated hemoglobin (SNO-Hb) may account for the failure of RBC transfusion to acutely restore tissue oxygen delivery.[3]

Methods: The primary goal was to measure and analyze variation of SNO-Hb levels in autologous whole blood stored in citrate-phosphate-dextrose (CPD) solution for up to eight hours at room temperature. Whole blood harvested during intraoperative normovolemic hemodilution was sampled at two time points: 1) immediately after collection of blood into CPD solution, and 2) just prior to reinfusion of the harvested whole blood four to seven hours later. The samples were processed according to a protocol using photolysis-chemoluminescence-based NO detection.

Results: SNO-Hb levels measured within 15 min after collection into CPD solution were 0.00073 +/- 0.00021 moles SNO per mole Hb (mean and SEM, n=8), comparable to values reported previously by our group and others in fresh blood. In contrast, when assayed again just prior to reinfusion (4-7 hours later), SNO-Hb levels had fallen significantly (0.00031 +/- 0.00016 moles SNO/mole Hb; p=0.038).

Total Hb-bound NO (0.00273 +/- 0.00022 moles NO/mole Hb) and iron nitrosyl hemoglobin (Hb[Fe]NO, in which NO is bound to Hb's heme iron groups, 0.00200 +/- 0.00088 moles NO/mole Hb), both basally and at reinfusion, were substantially higher than in published reports in awake normal humans. The reason for this novel finding is unclear, but may reflect upregulated NO synthase activity secondary to inhalational anesthesia. No differences were found between the initial and reinfusion points for either total Hb-bound NO or Hb[Fe]NO (p=0.09 and p=0.79, respectively).

Conclusion: When measured in harvested autologous whole blood stored in CPD solution for up to seven hours at room temperature, SNO-Hb levels fell significantly. Reduced levels of SNO-Hb may cause "fresh whole blood" to behave more like banked RBCs, resulting in reduced tissue microvascular perfusion and reduced tissue oxygen delivery in spite of enhanced oxygen carrying capacity.

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DEVELOPING A CONGENITAL HEART ANESTHESIA DATABASE: COOPERATION TOWARDS BETTER OUTCOMES

Vener, M.D. D

Baylor College of Medicine / TCH

In 2005, the Congenital Cardiac Anesthesia Society (CCAS) was formed to serve as an informational and educational conduit for anesthesia providers taking care of children and adults with congenital heart defects. A major priority for the CCAS is establishing a multi-site database. Anesthesia complications are rare, but reviews show that patients with congenital heart defects (CHD) have up to 85x greater risk of serious complications while undergoing all types of procedures.(1,2) A multi-site database allows contemporaneous collection of sufficient numbers of patients to allow for timely analysis of CHD treatments and anesthesia-related complications.(3)

The CCAS has elected to join the Society of Thoracic Surgery's Congenital Heart Surgery Database and utilize the extensive work already done by that organization in diagnosis and procedural definitions. Beginning with the 2010 data collection, the STS-CCAS collaboration has added anesthesia-related fields (see attached Data Collection Form). The STS-CCAS database has been expanded to allow for anesthesiologists to add data from outside the Cardiac ORs for diagnostic and interventional catheterizations, radiology imaging, and non-cardiac surgical procedures on CHD patients.

Another feature in the 2010 database is the Unique Patient Identifier. This will allow for a patient's course to be tracked across multiple institutions in a longitudinal fashion, since many CHD patients have multiple procedures at multiple locations. This information will also be utilized to cross-reference with the Social Security and state death records to ascertain mortality data that would otherwise be unreliable or unavailable.

For this database to be effective, anesthesia departments and hospitals will have to invest significant resources to support these efforts. However, this data will be critical in showing the efforts we are making to improve anesthesia-related outcomes and may guide future care. The SCA and ASA have budgeted millions of dollars towards Quality Institutes and Initiatives that will likely involve similar database efforts. For individual physicians, participation in this type of database may be useful in Maintenance of Certification (MOCA) activities required by the American Board of Anesthesiology for ongoing recertification.

It is anticipated that data collection will begin January 1, 2010, with the first harvest occurring in Spring 2011.

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DIRECT INTERSTITIAL MEASUREMENTS OF TRANEXAMIC ACID REVEALS ORGAN SPECIFIC HETEROGENEITY IN PHARMACOKINETIC PROFILES

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

Medical University of South Carolina

Background: Currently, a pharmacological mainstay to manage post-operative bleeding in the context of cardiac surgery is through antifibrinolytic therapy using lysine analogues such as tranexamic acid (TXA). However, an empirical weight based dosing regimen is most commonly utilized, and whether and to what degree differences in localized accumulation of TXA occur in specific tissue compartments using this intravenous dosing regimen remains to be established.

Methods: Adult pigs (30 kg; n=9) were instrumented with microdialysis catheters placed in the left ventricular myocardium, renal parenchyma, quadriceps muscle, and left central lobe of the liver. Microdialysis was performed and interstitial fluid (100 uL) collected under steady-state conditions for each compartment at baseline, 30, 60, 90 and 120 minute intervals following TXA infusion (30mg/kg). The samples were then separated by high pressure liquid chromatography and TXA concentrations measured by an internally calibrated tandem mass spectrometry method. Thus, absolute interstitial profiles could be determined for each compartment whereby peak TXA concentration values (peak-TXA), as well as the area under the TXA-time concentration curve (TXA-AUC; [mcg/mL]xmin) could be computed.

Results: The TXA-time interstitial concentration curves for each compartment are shown in Figure 1. Peak-TXA values occurred at 30 minutes post infusion, and were 5-fold higher in the renal compartment and 3-fold higher in the myocardium, when compared to the liver or muscle; both $p < 0.05$. Moreover, the TXA-AUC was highest in the renal compartment (529+134) when compared to the liver (152+32) or muscle (115+33); both $p < 0.05$. The TXA-AUC was higher in the myocardium (304+33) when compared to the liver (152+32) or muscle (115+33); both $p < 0.05$.

Conclusions: Using a large animal model and direct in-vivo microdialysis measurements of TXA concentrations, the unique findings from this study were 2-fold. First, intravenous TXA infusion results in a heterogeneous distribution of peak concentrations within organs systems relevant to cardiac surgery (renal, myocardium). Second, the significant peak interstitial levels of TXA as well as the increased AUCs in the kidney and myocardium may alter local fibrinolytic pathways to a greater degree. Thus, a single weight based dose of TXA can cause significant and unanticipated interstitial accumulation in the kidney and myocardium which may have undesired consequences in the context of antifibrinolytic therapy in cardiac surgery.

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EARLY EXTUBATION IN CONGENITAL HEART SURGERY – A MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY AND RISK SCORE ASSESSMENT.

Mittnacht A; Rhee A; Kin N; Weisman C; Hossain S; Bodian C; Nguyen K; Hollinger I

The Mount Sinai Medical Center; The University of Tokyo Hospital

Background: Extubation in the operating room (OR) after surgery for congenital heart disease (CHD) can be achieved in patients who are not mechanically ventilated preoperatively.

Objective: The goal of this study was to identify perioperative factors associated with the decision to not proceed with planned OR extubation, and to develop a risk score for early extubation following CHD surgery.

Methods: Prospective observational study of 275 pediatric patients undergoing CHD surgery using cardiopulmonary bypass (CPB) at the Mount Sinai Medical Center (MSMC). Inclusion criteria were; age 2 weeks-18 years old, no preoperative ventilatory support, and Inotrope Score \leq 20. General anesthesia was supplemented with a single shot caudal or intrathecal morphine in all patients. For the univariate analyses, the Chi-square or the Fischer's Exact Tests were used as appropriate. A Chi-square Test for trend was used to test for linear association. The independent influence of various patient and perioperative characteristics on outcome was tested using a Stepwise Logistic Regression. We developed a simple risk score based on the results of the Logistic Regression, and applied them to prospectively obtained data from another institution (49 pediatric patients undergoing surgery for CHD at The University of Tokyo Hospital).

Results: The majority of patients (89%) were extubated in the OR following surgery for CHD at the MSMC. All low risk surgical patients (RACHS 1) and patients without aortic cross-clamping were extubated in the OR. Multiple regression analysis of the remaining 184 patients showed that Down's syndrome, age, and surgical risk (RACHS score) were independent predictors for not extubating in the OR. Our risk score model is presented in Table 1. The overall OR extubation rate at The University of Tokyo was 65% (32/49). Our risk score model was able to predict patients at low, intermediate, and high risk of failure of such an early extubation strategy.

Conclusion: Operating room extubation after surgery for CHD can be safely accomplished in the majority of appropriately selected patients. Our pediatric extubation risk score model can be used to predict early extubation after CHD surgery.

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EFFECT OF INOTROPIC SUPPORT ON HEMODYNAMIC AND BI-VENTRICULAR FUNCTION IN PATIENTS UNDERGOING VALVULAR SURGERY.

André A; Couture P; Beaulieu Y; Shi Y; Nozza A; Pagé P; Tardif J; Lambert J; Rochon A

Montreal Heart Institute

Background: Inotropic agents are often needed to wean from cardiopulmonary bypass (CPB) in valvular or complex surgery (1), but their effects on systolic and diastolic function has not been well reported (2). The aim of this study was to evaluate the effect of inotropic support on bi-ventricular systolic and diastolic function, as well as outcome, compared to a control group without inotropes, in patients undergoing valvular surgery.

Methods: Single-center double-blind, double-dummy, randomized controlled trial in patients undergoing valvular surgery and randomized to receive intravenous amiodarone or placebo intraoperatively. Patients were divided in those requiring or not post-operative inotropic agents. Demographic and biochemical data were obtained. Hemodynamic profile and bi-ventricular comprehensive transesophageal echocardiographic (TEE) exam were performed and described before, after bolus and after cardiopulmonary bypass (CPB). Patients were followed-up for 6 years. The chi-square test was used to assess group differences. Unpaired t-test and repeated measures ANOVA models were used to study the hemodynamic and echocardiographic parameters. The generalized estimating equation (GEE) model was performed to study ventricular diastolic function. Multivariate logistic regression was used to identify the independent predictors of the use of inotropes. To evaluate the long-term effect of inotropes treatment on mortality, a log-rank test was performed. A p value ≤ 0.05 was considered significant.

Results: One hundred and twenty patients (mean age 65 ± 11 years) were randomized to amiodarone or placebo. There was no difference in the use of inotropic agents after CPB in patients randomized to amiodarone or placebo. There were no significant baseline hemodynamic differences among patients receiving inotropes after CPB. Patients receiving inotropes after CPB had increased left atrial dimensions ($p = 0.0196$), increased E/e ratio ($p = 0.0104$), reduced tissue Doppler mitral systolic velocities ($p = 0.0086$), increased end-systolic right ventricular area dimension ($p = 0.0197$) with associated reduced hepatic venous flow systolic velocities ($p = 0.0093$) before CPB. Inotropic agents after CPB were associated with increased tissue Doppler mitral annular atrial velocities ($p = 0.0252$), pulmonary ($p = 0.0459$) and hepatic venous flow ($p = 0.003$) atrial reversal velocities. There were no difference in post-operative complications and in survival in both group however the number of death at 6 years was increased in patients who received intraoperative inotropes ($p = 0.0247$).

Conclusion: In patients undergoing cardiac valvular surgery, significant hemodynamic and bi-ventricular systolic and diastolic echocardiographic changes do occur after CPB. Inotropic medications were not associated with a difference in hemodynamic and echocardiographic parameters after CPB when compared to a control group except for an increase in bi-atrial activity after CPB. At 6 years, despite similar baseline demographic characteristics, an increased number of deaths was observed in patients requiring inotropic medication.

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EFFECT OF INTRAVENOUS AMIODARONE ON HEMODYNAMIC AND BI-VENTRICULAR SYSTOLIC AND DIASTOLIC FUNCTION DURING VALVULAR SURGERY

Denault A; Beaulieu Y; Couture P; Shi Y; Pagé P; Levesque S; Tardif J; Lambert J; Deschamps A

Montreal Heart Institute

Background: Atrial fibrillation (AF) is a common complication after cardiac surgery. Postoperative AF is associated with increased risks of morbidity and mortality, and preventive strategies using amiodarone are more commonly used during cardiac surgery (1,2). However the effect of intravenous amiodarone administered intraoperatively on hemodynamic and biventricular echocardiographic parameters using transesophageal echocardiography (TEE) have not been described in patients undergoing valvular or complex surgery.

Methods: Single-center double-blind, double-dummy, randomized controlled trial in patients undergoing valvular surgery. Patients received either an intravenous (IV) loading dose of 300 mg of amiodarone or placebo in the operating room, followed by a perfusion of 15 mg/kg per 24 hours for 2 days. Hemodynamic profile and bi-ventricular comprehensive TEE exam were performed and described before, after bolus and after cardiopulmonary bypass (CPB). Postoperative complications and mortality at 6 years were also documented. Chi-square tests were used to compare categorical variables between groups (with or without amiodarone). For continuous variables, the Student t-test or Wilcoxon test were used to compare groups. To analyze the evolution of the variables, mixed-model repeated-measures analyses of covariance controlling for the baseline value were used. These analyses were performed with SAS 8.02 (SAS Institute Inc., Cary, North Carolina). The Wilcoxon test was used to compare the distribution of frequencies of both left and right ventricular diastolic function patterns. A P value less than .05 was considered statistically significant.

Results: One hundred and twenty patients (mean age was 65 ± 11 years) were randomized to amiodarone or placebo. The placebo group had more patients with diabetes ($p=0.0244$) and longer duration of CPB ($p=0.0426$) while the patients in the amiodarone group had more frequent isolated valvular procedures ($p=0.0497$). There was no difference in the use of inotropic agents after CPB in either group but the amiodarone group required more frequently temporary pacing for bradyarrhythmia up to 24 hours ($p=0.0075$). After the bolus, the amiodarone group increased their mean pulmonary artery pressure ($p=0.0450$) with associated reduction in S/D ratio of the hepatic venous velocity ($p=0.0457$). After CPB a lower heart rate ($p<0.0001$) and lower cardiac index ($p=0.0157$) was observed in the amiodarone group with higher diastolic pulmonary venous flow velocities ($p=0.0052$). There were no differences in post-operative complications and in survival in both groups at 6 years.

Conclusion: In patients undergoing cardiac valvular surgery, intravenous amiodarone is well tolerated hemodynamically and not associated after CPB with significant changes in systolic and diastolic function and does not increase inotropic requirement when compared to placebo despite a reduction in heart rate, cardiac index and increased pacemaker requirement for 24 hours.

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EFFECTS OF RENIN ANGIOTENSIN INHIBITORS ON THE OCCURRENCE OF ACUTE KIDNEY INJURY AFTER OFF-PUMP CORONARY ARTERY BYPASS GRAFTING

Yoo Y; Shim J; Kim J; Ahn S; Kwak Y

Yonsei University College of Medicine; Yonsei University College of Medicine,

Background: Angiotensin converting enzyme inhibitors (ACEi) and angiotensin II type 1 receptor antagonists (ARBs) are known to reduce cardiovascular events and widely used in high-risk patients with cardiovascular disease. Although the use of ACEi or ARBs delay the progression of renal disease, they also reduce glomerular perfusion pressure. Although there were some studies to determine the renal effects of ACEi or ARBs in patients undergoing cardiac surgery^{1,2} but no final conclusions are available, and no previous study has demonstrated the renal effect of ACEi or ARBs after off-pump coronary artery bypass grafting (OPCAB). The aim of the present study is to determine the effect of ACEi or ARBs on renal function after OPCAB.

Method: A total of 399 patients including patients received ACEi or ARBs for at least 3 weeks and underwent OPCAB were reviewed. Patients with chronic renal failure were excluded. One hundred forty four patients did not receive any ACEi or ARBs (control group), 122 patients received ACEi (ACEi group), and 105 patients received ARBs (ARB group). The primary end point was the incidence of acute kidney injury (AKI). AKI was defined as increase in serum creatinine over 0.3 mg / dl or increase of 50% from baseline. Estimated glomerular filtration rate (GFR) and creatinine clearance (CrCl) at post operative day (POD) 0, 1, 2 and 7, and postoperative outcomes were compared between the three groups.

Result: Demographic data including preoperative acute renal failure scorings and operative data were similar. Occurrence of AKI (17.4% vs 19.7% vs 18.1%, $P = 0.886$) was comparable. There were no significant differences in GFR and CrCl at POD 0, 1, 2 and 7 between the groups. Postoperative outcomes were also similar between the groups (Table1).

Conclusion : Preoperative chronic use of ACEi or ARBs did not significantly affect postoperative renal function and not increase the incidence of postoperative ARF in patients undergoing off-pump CABG.

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EFFICACY OF LOW TIDAL VOLUME VENTILATION DURING ONE LUNG VENTILATION

Chung P; Veksler B; Kraidin J; Solina A; Grubb W; Ginsberg S; Deangelis V; Denny J; Pantin E; Langenfeld J

UMDNJ Robert Wood Johnson

Objective: To determine if 5ml/kg tidal volume could maintain an oxygen saturation of at least 91% during anesthesia with one lung ventilation.

Design: Prospective study

Setting: A single institution, teaching hospital

Participants: Thirty-seven patients undergoing surgery requiring one lung ventilation, captured during the three month study period.

Interventions: Tidal volumes of 5ml/kg were instituted upon lung isolation using volume controlled ventilation. If, using volume control, peak pressures exceeded 30 cmH₂O then pressure controlled ventilation was implemented.

Addition PEEP and CPAP were used if the saturation fell to 91% while using low tidal volumes. If oxygen saturation greater than 91% could not be maintained without increase in tidal volume to 10ml/kg, then that subject failed.

Measurements and Main Results: With tidal volumes set to 5ml/kg the lowest mean oxygen saturation measured by pulse oximetry was 95.64%; the 95% confidence interval was 94.2% to 97.78%. The failure rate to maintain a saturation of 91% or better was 3%; the 95% confidence interval was 13%.

Conclusions: We were able to show that low tidal volumes for one lung surgery were able to allow the successful and safe completion of surgery. Adequate oxygenation was maintained with an average of 95%, and the failure rate was 3%.

EFFICACY OF OLPRINONE CHLORIDE IN PEDIATRIC CARDIAC SURGERY FOR CONGENITAL HEART DISEASE

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

Tokyo Women's Medical University

Introduction

Olprinone chloride (Olp) is a phosphodiesterase inhibitor available in Japan from April 1996. It has been reported that Olp produced reduction of systemic vascular resistance and increase of cardiac index after pediatric cardiac surgery in ICU. However, no data are yet available at weaning from cardio-pulmonary bypass (CPB) during pediatric cardiac surgery. The aim of this study is to clarify the time course of the blood concentration (BC) elevation of Olp and the effects of Olp on hemodynamics and oxygen delivery when Olp is administered at weaning from CPB.

Methods

Sixteen patients were enrolled in this study. A PediaSat central venous catheter was placed in the superior vena cava to measure the venous oxygen saturation (ScvO₂) continuously during the surgery and the cerebral tissue oxygen index (TOI) was monitored by NIRO in all of the patients. In majority of cases, INVOS probes were attached to the forehead to measure cerebral regional tissue oxygen saturation (rSO₂).

An Olp infusion of 0.3 mg/kg/min was started immediately after the release of aortic cross-clamping (ACC) without loading dose. When ACC was not applied, infusion was started immediately after the surgical procedure was completed. The simultaneous infusion of inotropes and vasodilators was not prohibited. The selection and infusion doses of these agents were basically left to the discretion of the attending anesthesiologists.

The BC was measured at 15, 30, 60, 90 and 120 minutes (min) after the beginning of the infusion, and also at same time interval after separation from CPB (sep-CPB). Hemodynamic data were collected from sep-CPB up to 12 hours after the ICU admission. Base excess (BE) and lactate were measured immediately and about 2 hours after sep-CPB, and repeatedly on arrival and 2, 6, and 12 hours after admission to ICU.

Repeated ANOVA followed by post hoc test and paired t-test were used for statistical analysis and P<0.05 was considered significant.

Results

The effective BC of Olp was achieved from 60 min after commence of infusion, and from 30 min after sep-CPB. While heart rate was not influenced, blood pressure increased from 30 min after sep-CPB. The inotrope doses were tapered significantly from 60 min after sep-CPB. ScvO₂ and the oxygen excess factor (OEF) tended to increase from 15 min after sep-CPB, and OEF significantly increased at 30 min. The changes of cerebral rSO₂ and TOI resembled those of ScvO₂ and OEF; in trend, and TOI significantly increased at 15 and 90 min. BE and lactate did not change during the early period after sep-CPB. The hemodynamic parameters were stably maintained from soon after the ICU admission without any declines of BP with any suspected causal relation to the olprinone infusion. No sign indicative of a deterioration of the balance between the oxygen supply and oxygen demand was observed in ICU.

Conclusion

With a continuous infusion of Olp at 0.3 mg/kg/min started after the release of ACC, the BC reached to the effective concentration by 30 min after sep-CPB. Concurrently with the achievement of the effective BC, the circulation was stabilized and the oxygen delivery was improved.

EVALUATION OF AN ONLINE TEACHING AID FOR STANDARD TRANSESOPHAGEAL ECHOCARDIOGRAPHY VIEWS

Jerath A; Vegas A; Meineri M; Michael C; Gordon T; Christopher F

Toronto General Hospital

Introduction

Transesophageal echocardiography (TEE) is a commonly used perioperative cardiac imaging modality used by cardiologists, anesthesiologists, cardiac surgeons and intensive care physicians. It is widely used to assess cardiac structure, function, pathology and surgical intervention. Novices studying TEE are challenged by translating the anatomical information and terminology of the 20 standard views to the 3D model of the heart. We have developed an online application that allows users to visualize all 20 standard views in conjunction with a 3D heart model that can be rotated and 'cut away' above the echo plane revealing the internal cardiac structures. The purpose of this study was to assess whether the application was a useful educational tool and to rate user satisfaction.

Methods

We devised two 20 question multiple choice exams based on the standard views assessing the recognition of anatomical structures and type of view. The tests were validated by determining their ability to discriminate between novice, intermediate and experienced echocardiographers. We measured the performance improvement in 10 postgraduate trainees, 4 anesthesiologists, 3 cardiologists and 3 cardiac surgeons. Each completed one exam before (pre-test) and a second exam (post-test) after having 3 days of unlimited access to the TEE application. The order of the 2 exams was randomized. We recorded the number of years of postgraduate and TEE experience, duration the application was used and satisfaction scores. Parametric data is recorded as mean +/- standard deviation and analysed using a paired t-test. A p value < 0.05 was considered significant. User satisfaction was recorded using the 5 point Likert scale (1=strongly disagree, 5=strongly agree).

Results

Seven trainees had 6 or more years, 2 with 5 years and 1 with 4 years of postgraduate experience. Six candidates had no previous TEE experience and 4 had only performed case studies. The pre-test score was 51% +/- 0.12, post-test score 82% +/- 0.15 with a mean improvement of 31% +/- 0.16, $p < 0.001$, see table 1. Duration the application was used over the 3 days was 133 +/- 109.6 minutes with a mean number of 3.9 sessions. Satisfaction scores rated highly, ranging between 4.4 - 4.9, see table 2.

Discussion

This virtual TEE application proved to be a fast, simple teaching tool to enhance the performance and understanding of TEE among trainees from various medical disciplines. This application is now freely available online (<http://pie.med.utoronto.ca/tee>) and is being accessed by over 1000 people/month, complimenting the traditional textbook and bedside teaching modes of learning the fundamentals of TEE.

EVALUATION OF THE EFFECTS OF FRESH FROZEN PLASMA FOR PUMP PRIMING IN PEDIATRIC PATIENTS UNDERGOING CONGENITAL HEART SURGERY USING COAGULATION FACTOR ASSAY AND ROTATIONAL THROMBOELASTOGRAM

Kim J; Lee J; Shim J; Ahn S; Yoo Y; Kwak Y

Yonsei University College of Medicine

Background

Dilutional coagulopathy with relatively larger priming for pediatric cardiopulmonary bypass (CPB) has been a challenging task of postoperative care for congenital heart surgery. Management for adequate hemostasis is not yet standardized. The aim of this prospective, randomized study was to evaluate the hypothesis that fresh frozen plasma (FFP) given into pump priming could improve the postoperative coagulation profile in pediatric patients undergoing cardiac surgery with CPB.

Methods

67 patients, aged 1 month to 18 yr, undergoing elective congenital heart surgery with CPB were randomly assigned to either control (C) or treatment (T) group, given 10% albumin or FFP for pump priming, respectively. Coagulation assays, including platelet, fibrinogen level, PT, aPTT, and rotational thromboelastogram (ROTEM), were checked as follows: after anesthesia induction (baseline), after CPB discontinuation & heparin reversal (post-CPB weaning), and 24 hours after ICU admission (postoperatively). Weight-standardized amounts of intraoperative surgical bleeding, chest tube drainage during 24 h of ICU stay, and perioperative transfusion requirement were measured.

Decision-making for postoperative care including transfusion was at discretion of physicians blinded to the patient assignment.

Results

No specific differences were found for demographic data between groups. For patients undergoing initial surgery, post-CPB weaning fibrinogen level was significantly higher in T group [190 ± 36.9 vs. 119.4 ± 35.7 , $p < 0.0001$]. Moreover, clot strength was shown to be enhanced in T group [76.4 ± 19.9 vs. 56.6 ± 18 , $p < 0.05$], as indicated by ROTEM parameter of MCE (maximal clot elasticity). The intraoperative blood transfusion was larger in T group, probably due to FFP [55.4 ± 29.6 vs. 75.2 ± 38.1 , $p < 0.001$]. In the ICU, however, more FFP was given in C group [33.9 ± 49.2 vs. 19 ± 61 , $p = 0.035$]. Transfusion requirement during 24 h after ICU admission was nearly doubled in C group, but without significance [18.9 ± 34.5 vs. 7.8 ± 13.9]. Chest tube drainage during ICU stay was significantly larger in C group [16.9 ± 20.7 vs. 10.4 ± 8.2 , $p < 0.05$]. For patients undergoing repeated sternotomy, FFP priming significantly reduced the intraoperative bleeding [18.3 vs. $12.5, 18.5$] vs. 9.9 vs. $5.2, 10.9$, $p = 0.004$], and transfusion requirement in ICU [22 vs. $15, 48.3$] vs. 9.2 vs. $5.3, 18.6$]. But limited number (9 and 10 for C & T group, respectively) of the repeated surgery patients enrolled for this study could lessen the statistical power.

Conclusion

FFP priming for pediatric patients undergoing CHD surgery with CPB was demonstrated to enhance the clot strength just after CPB weaning, thereby reducing the bleeding & transfusion requirements during ICU stay especially in the patients undergoing repeated sternotomy.

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HEPARIN ATTENUATES THE HYPOTENSIVE EFFECT ASSOCIATED WITH HEPARIN-ANTAGONIST PMX-60056

McAllister E; Scott R; Korczak B; Stafford-Smith M

Duke Heart Center; PolyMedix Inc.; PolyMedix, Inc.

Background: PMX-60056 is a new small molecule developed from first principles to antagonize the anticoagulant effect of heparin. Initial studies in man were limited by dose-related hypotension that was transient but undesirable; average systolic (sbp) and diastolic (dbp) blood pressure reductions of 35% and 45% that were observed with 0.5mg/kg recovered over 30 minutes. However doses of 0.1 and 0.2mg/kg did not result in clinically relevant hypotension. Since PMX-60056 combines rapidly and irreversibly with heparin, hypotensive effects associated with unopposed drug may not accurately reflect the clinical safety profile of PMX-60056 in the presence of heparin. Therefore we tested the hypothesis that 0.3mg/kg PMX-60056 in heparin-anticoagulated subjects would not be associated with hypotensive responses seen with unopposed agent.

Methods: With IRB approval and informed consent, six volunteer male subjects participated in this double-blind randomized placebo-controlled crossover trial. Subjects received 70U/kg heparin by intravenous bolus then, after 20 minutes, a 10 minute infusion of either PMX-60056 or placebo. Point of care anticoagulation testing and hemodynamic data, including heart rate, sbp and dbp (by automated brachial arm cuff) were obtained prior to drug infusion, at 2, 5, and 9 mins during, and 2, 5, 10, 20, 60, and 240 mins after the infusion. After a 2-day washout the second arm of the protocol was performed in a similar fashion. All subjects were observed from the day prior to the day after completion of the protocol. The nadir sbp/dbp values following completion of study drug for each subject were averaged for comparison with values immediately preceding the study drug, using a 2-sample paired t-test, $p < 0.05$ was considered significant.

Results: Mean sbp and dbp values are depicted (Figure). Nadir sbp/dbp were not significantly different from baseline for placebo, while nadir sbp/dbp values of 10.5 and 11.0mmHg respectively reflected a modest but significant blood pressure drop with PMX-60056 (8.9 and 14.7%, respectively) (Table). The table shows mean maximum reductions with 95% confidence intervals (CIs) for the absolute values. No subjects had symptomatic hypotension at any time.

Conclusions: Blood pressure declines observed after heparin-anticoagulated individuals receive 0.3mg/kg PMX-60056 are modest compared to placebo, and attenuated compared to those observed in non-anticoagulated individuals receiving (unopposed) 0.5mg/kg PMX-60056. Preliminary point of care anticoagulation assessments indicate that 0.3 mg/kg PMX-60056 exceeds reversal requirements for the 70 U/kg heparin study protocol dosing.

Maximum BP Drop	Maximum BP drop				
PMX-60056 %	mmHg [95%CI]	Placebo	%	mmHg [95%CI]	
Systolic 8.90%	10.5 [1.4,19.6]	Systolic -0.80%	-1.0	[-5.1,3.1]	
Diastolic 14.70%	11 [1.9,20.0]	Diastolic 1.90%	1.5	[-0.7,3.7]	

HYPOXIA INDUCED DECREASE IN URINE OSMOLALITY: AN EARLY SIGN OF RENAL INJURY WHICH IS AMELIORATED BY DDAVP

Voicu L; Mazer D; Hare G; Cheema-Dhadli S; Halperin M; Pang V; Kim N

St Michael's Hospital

Introduction: Acute kidney injury (AKI) is strongly associated with excess length of stay, morbidity, and mortality after cardiac surgery. The renal medulla is a central target for renal injury, likely because of its limited blood-oxygen supply and high metabolic requirements. The objective of this study was to identify an early physiologic diagnostic indicator of renal dysfunction in an in vivo model of hypoxic renal injury, and to determine if it could be prevented by administration of drugs such as dDAVP.

Methods: After institutional approval, adult male Sprague-Dawley rats (400-450g; n= 6-8/group) were fed a low electrolyte diet to approximate human Na⁺ consumption and housed in metabolic cages for 7 days. On day 3, rats were given an oral NaCl supplement and then exposed to either a hypoxic (FiO₂=8% O₂) or normoxic (FiO₂=21% O₂) environment for 5 hours. Samples of urine and plasma were collected and analyzed up to 72h after hypoxic or normoxic exposure. Additional groups of hypoxic or normoxic rats were treated with a long acting vasopressin analog (dDAVP: 2 µg ip x 2 doses) prior to hypoxia exposure. The primary outcomes were urine and renal papillary Na⁺, K⁺, and osmolality. Hypoxia inducible factor-1 (HIF-1) and neuronal nitric oxide synthase (nNOS) in renal tissue were measured using Western blot, and plasma erythropoietin (EPO) was measured using ELISA. Data is reported as means ± SD, with p<0.05 considered significant.

Results: Exposure to 8% O₂ caused a fall in PaO₂, elevated plasma lactate (3.1 ± 1.3 mM) increased plasma EPO (16 ± 6 vs 727 ± 856 pg/ml), and higher medullary HIF-1 (2.4-fold) and nNOS (3.7-fold) protein expression (p<0.05 for all). In hypoxic rats not treated with dDAVP, urine osmolality after 5 hours of hypoxia was significantly lower than normoxic rats (2447 ± 250 vs 925 ± 694 mOsm/kg H₂O, p<0.05). By contrast, dDAVP ameliorated the fall in urine osmolality at the end of hypoxia (2253 ± 742 mOsm/kg H₂O). The papillary osmolality was not significantly different from the urine osmolality in either group of hypoxic rats. In addition, dDAVP prevented the increase in Na⁺ and K⁺ excretion observed 6h after hypoxia (17 ± 9 versus 5 ± 2 in mmol/mmol creatinine and 9 ± 6 versus 2 ± 2 mmol/mmol creatinine respectively). dDAVP also ameliorated the rise in EPO (370 ± 193 pg/ml), and renal medullary HIF-1 and nNOS expression, suggesting it may have improved medullary tissue hypoxia.

Discussion: Hypoxia caused a fall in renal outer medullary function (low interstitial osmolality, higher Na⁺ excretion), which was prevented by pre-treatment with dDAVP. A decrease in urine osmolality may be of diagnostic value for hypoxic renal injury, and dDAVP may have prophylactic or therapeutic potential in patients at risk of AKI in the perioperative setting.

IMPAIRED AUTOREGULATION OF CEREBRAL BLOOD FLOW DURING RE-WARMING FROM HYPOTHERMIC CARDIOPULMONARY BYPASS AND ITS POTENTIAL ASSOCIATION WITH STROKE

Panigrahi R; Joshi B; Brady K; Hogue C

The Johns Hopkins University School of Medicine

Background: Re-warming after hypothermic cardiopulmonary bypass (CPB) has been linked to perioperative brain injury. The purpose of this study was to evaluate whether cooling and then re-warming of body temperature during CPB is associated with alterations in CBF-blood pressure autoregulation.

Methods: One hundred twenty-seven adult patients undergoing CPB had transcranial Doppler (TCD) monitoring of middle cerebral artery blood flow velocity (MCA-FV). Eleven patients undergoing "warm CPB" (arterial inflow $>35^{\circ}\text{C}$) served as controls. The mean velocity index (Mx) was calculated as a moving, linear correlation coefficient between slow waves of MCA-FV and mean arterial pressure (MAP). Intact CBF-blood pressure autoregulation is associated with an Mx that approaches zero. Impaired autoregulation results in an Mx approaching 1.0. Time-averaged Mx values were compared between before CPB (baseline), during the cooling and re-warming, and after CPB. The number of patients in each phase with an Mx ≥ 0.4 , indicative of impaired CBF autoregulation, was determined. **RESULTS:** During cooling, Mx [left, 0.29 ± 0.18 ; right, 0.28 ± 0.18 (mean \pm SD)] was greater than that at baseline (left, 0.17 ± 0.21 ; right, 0.17 ± 0.20 , $P < 0.0001$) (Figure). Mx increased during re-warming (left, 0.40 ± 0.19 ; right, 0.39 ± 0.19) compared with baseline ($P < 0.001$) and the cooling phase ($P < 0.0001$), indicating impaired CBF autoregulation. After CPB Mx (left, 0.27 ± 0.20 ; right, 0.28 ± 0.21) was higher than baseline (left, $P = 0.0004$; right, $P = 0.0003$), no different than during cooling, but lower than during re-warming (left, $P < 0.0001$; right, $P < 0.0005$). Forty-three (34%) and 68 (53%) patients had an Mx ≥ 0.4 during the cooling phase and re-warming, respectively. Nine of 11 Warm Controls had an average Mx ≥ 0.4 during the entire CPB period. There were 9 strokes all in patients with high Mx during re-warming. The unadjusted odds ratio for any neurologic event (stroke or transient ischemic attack) for patients with Mx ≥ 0.4 during re-warming was 4.1 (95% CI, 1.8 to 9.5, $P < 0.001$).

CONCLUSIONS: Hypothermic CPB is often associated with abnormal CBF-blood pressure autoregulation that is worsened with re-warming. We found a high rate of strokes in patients with evidence of impaired CBF autoregulation. Whether a pressure-passive CBF state during re-warming is associated with risk for ischemic brain injury requires further investigation.

INDEPENDENT RISK FACTORS FOR FAST TRACK FAILURE IN CARDIAC SURGERY PATIENTS

Ender J; Lindner J; Scholz M; Mukherjee C; Bless B; Mathioudakis D; Haentschel D

Heartcenter, University Leipzig; University Leipzig

Introduction: Fast track treatment of cardiac surgery patients is meanwhile a well established method mostly realised in the intensive care unit (ICU). Fast track failure is reported to appear in 15.6% of the patients (1). Two years after implementation of our fast track protocol using a post anesthetic care unit (PACU) to bypass the ICU completely. We evaluated retrospectively rate and reasons for fast track failure of our patients.

Method: After approval by the local ethic committee and based on the data of our clinical information system all patients from January 2007 until December 2008 who were treated in the PACU after major cardiac surgery were retrospectively reviewed. We were looking for fast track failure and comorbidities who could be responsible for the fast track failure. Fast track failure was defined as unplanned transfer of the patient from the PACU to the ICU and not to the step down unit for further treatment. First a univariate logistic regression analysis was performed using parameters judged as risk factors for fast track failure (1) like EuroScore, age, sex, ejection-fraction, myocardial infarction, impaired renal function, COPD, diabetes, re-operations, neurological comorbidity, pulmonary hypertension, peripheral artery disease, duration of cardiopulmonary bypass, cross clamp time and total operation time. Those factors significant in the univariate regression analysis were used for multivariate logistic regression analysis to look for independent risk factors for fast track failure.

Results: 1704 patients with a mean age of 63 ± 13 years were included in this retrospective study. Fast track failure occurred in 131 patients (7.7 %). The overall 30 days mortality was 1.1 %. In the univariate logistic regression analysis the factors log Euroscore, age, operation time, cross clamp time, sex and diabetes were significant risk factors. In the multivariate regression analysis age over 70 years (odds ratio OR=2.2, $p < 0.001$), operation (OR=1.4 per hour, $p = 0.001$) as well as cross clamp time (OR=1.5 per hour, $p = 0.035$) and sex (OR=1.5, $p = 0.007$) are independent risk factors for fast track failure.

Conclusion: Fast track treatment in a post anesthetic care unit is safe and feasible also for elder patients. However, female patients with the age of > 70 years undergoing long lasting cardiac surgical procedures are at higher risk for fast track failure.

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INTRAOPERATIVE MULTISITE NEAR-INFRARED SPECTROSCOPY (NIRS) PREDICTS ELEVATED BLOOD LACTATE LEVEL IN PATIENTS UNDERGOING SURGERY FOR CONGENITAL HEART DISEASE.

Chakravarti S; Srivastava S; Nguyen K; Mittnacht A

The Mount Sinai Medical Center

Background: NIRS has been increasingly used to non-invasively measure regional tissue oxyhemoglobin saturation (rSO₂). Regional low rSO₂ values have been suggested to reflect impaired global tissue perfusion.

Objective: To determine if a relationship exists between regional oxyhemoglobin saturation (rSO₂) measured by near infrared spectroscopy (NIRS) at various body locations and blood lactate level in patients following congenital cardiac surgery.

Methods: Prospective, observational pilot study. Twenty-three patients (median age 6 month, range 3 days-27 years) undergoing repair of congenital heart disease. Patients with single ventricle physiology and/or residual intracardiac shunts were excluded. Cerebral, splanchnic, renal, and muscle rSO₂ were recorded every 30 seconds via NIRS from induction of anesthesia until end of surgery. Blood lactate levels were measured every 30 minutes. Length of time spent 10%, 20%, 30%, and 40% below baseline rSO₂ was determined. Pearson correlation coefficients were calculated in order to examine the relationship among lactate and rSO₂. Receiver operating characteristics curve analysis was used in order to determine the optimal combination of sites and the threshold rSO₂ value for the prediction of hyperlactataemia.

Results: Minimum rSO₂ value during surgery was not associated with intraoperative lactate levels. Prolonged (>40 minutes) cerebral and renal decrease (20%) from baseline was strongly correlated with intra-operative hyperlactatemia (increase in lactate > 3 mmol/L) with a sensitivity of 88% and a specificity of 100%.

Conclusion: A combination of cerebral and renal rSO₂ can be used to non-invasively predict hyperlactatemia as a marker of global hypoperfusion in patients undergoing surgical repair of congenital heart disease.

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INTRAOPERATIVE REAL-TIME THREE-DIMENSIONAL TRANSESOPHAGEAL ECHOCARDIOGRAPHY PROVIDED USEFUL INSIGHTS TO LEFT VENTRICULAR OUTFLOW TRACT MORPHOLOGY AND MITRAL SYSTOLIC ANTERIOR MOTION MECHANISM IN A HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY OPERATION

Nguyen H; Anthony D; Alfirevic A

Cleveland Clinic Foundation

INTRODUCTION:

Left ventricular outflow tract (LVOT) obstruction portrays a prognostic indicator in hypertrophic cardiomyopathy (HOCM) patients.¹ Septal myectomy improves functional status with elimination of LVOT obstruction.² Intraoperative real-time 3-dimensional transesophageal echocardiography (RT3D-TEE) can provide unique anatomic views of the dynamic LVOT obstruction in HOCM as well as more surgically specific and accurate measurements.

CASE REPORT:

65 years-old male with near-syncopal episode and exertional dyspnea presented with symptomatic HOCM. He was scheduled for an elective septal myectomy. Preoperative TEE by cardiology reported a septal thickness of 2.6 cm, severe elongated, redundant anterior mitral valve leaflet (AMVL), 2-3+ mitral regurgitation (MR) with posteriorly directed jet, and severe systolic anterior motion (SAM) of the MV with a dynamic gradient of 75mmHg at rest and 136mmHg after stress.

Intraoperatively, 2-D TEE confirmed preoperative findings. Performing RT3D-TEE image acquisition then ensued, using a phased-array 3-D matrix rendering an online imaging interfaced with a Phillips Sonos 7500 ultrasound machine. RT3D-TEE showed an elongated MV A2 scallop. More importantly, "cropping" techniques of the Live 3D-zoom enabled us to obtain short-axis LVOT views with "live" view of the exact location of the MV SAM. In addition off-line measurements obtained via the Q-lab enabled accurate 3D positioning and measurement of the septal wall thickness (Figure 1) as well as measurement of the LVOT area (Figure 2). Myectomy proceeded with MV A2 scallop plication. Post-myectomy, live 3D-zoom RT3D-TEE as well as Q-lab measurements of the LVOT area showed resolution of SAM. Peak gradient across the aortic valve was 28 mmHg.

DISCUSSION:

In this case, RT3D-TEE provided information about the geometry of LVOT, the mechanism of SAM and the location of the obstruction on the basal septum. RT3D-TEE live 3D visualization of the MV SAM. In addition, it facilitated 3D septal measurements and evaluation of the LVOT area during dynamic obstruction. RT3D-TEE rendered useful information before and after septal myectomy

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IS THE SYSTOLIC FUNCTION OF THE INTERVENTRICULAR SEPTUM ENHANCED AFTER REDUCTION OF ELEVATED RIGHT VENTRICULAR PRESSURE DURING CORRECTIVE SURGERY FOR CONGENITAL HEART DISEASE?

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

Tokyo Women's Medical University

Introduction

Abnormal motion and deformity in the shape of the interventricular septum (IVS) are well known manifestations in patients with elevated right ventricular pressure (RVp). Yet the characteristics of the IVS motion have not been clearly defined. Therefore, the purpose of this study is to clarify the characteristics of the systolic function of IVS in patients with elevated RVp, in comparison with the characteristics of the systolic function of the anterior wall (AW). We hypothesize that the IVS motion is reduced relative with the AW motion and will be improved after reduction of RVp, and that the time to peak motion at the IVS is inconsistent with that at the AW and will be synchronized after the reduction of RVp.

Methods

Eight pediatric patients with congenital heart disease accompanied with elevated RVp were enrolled in this study. Using 2D-tracking technology developed by Aloka Corporation, the endocardial circumferential strain at the AW and IVS were analyzed. The peak circumferential strain and time to peak were measured to compare between those at the AW and those at the IVS.

Transgastric left ventricle short axis views for 3 cardiac cycles were stored in ultrasound system during hemodynamic stability was achieved both after induction of anesthesia and after separation from cardiopulmonary bypass. The stored raw data were then analyzed off-line on personal computer using DAS-RS1 software.

Measurements were repeated for 3 times and averaged.

Paired t-test was used for statistical analysis and $P < 0.05$ was considered significant.

Results

The patients ranged from 4 to 53 months in age and from 4 to 14.5 kg in weight. Preoperative diagnoses were tetralogy of Fallot in 2, ventricular septal defect (VSD) with pulmonary hypertension in 3, VSD after pulmonary artery banding in 1, atrial septal defect with pulmonary stenosis (PS) in 1 and double outlet from right ventricle with PS in 1. Preoperative pressure ratios of the two ventricles (RVp/LVp) were moderate to severe in all of the cases. One of the cases showed over-systemic RVp.

Intracardiac repairs were performed in all of the patients. And reduction of the RVp was achieved in all of the cases immediately after the separation from CPB (an average of 42% reduction in RVp/LVp).

While the circumferential % strain at AW did not change at all, the % strain at the IVS tended to be enhanced after reduction of RVp, but not to a statistically significant degree. The ratio of the % strain at the IVS to AW, tended to be small, however, this tendency also fell short of statistical significance.

The time to peak at the AW and at the IVS were both accelerated, probably because of the increase in heart rate. The ratio of time to peak at the IVS to that at the AW was entirely unchanged.

Conclusion

Contrary to our hypothesis, our results indicated that systolic function of the IVS was not significantly enhanced after the reduction of RVp and that the time to peak systolic motion was not even minimally affected by the reduction of RVp. However, a further study in patients with elevated RVp and a comparison of these patients to patients with normal IVS function will be required to conclusively define the IVS function in patients with elevated RVp.

LOW DOSE DEXAMETHASONE DOES NOT AFFECT POST OPERATIVE NAUSEA AND VOMITING FOLLOWING CARDIAC SURGERY

Sherwani S; Patel K; Knorpp H; Gupta D; Murphy G

NorthShore University Health System; Northwestern University Feinberg School of Medicine

INTRODUCTION: Low dose dexamethasone is well known to decrease the incidence of nausea and vomiting postoperatively in noncardiac surgery. Only one study has investigated the use of low dose dexamethasone in cardiac surgery. In this study, patients randomized to receive dexamethasone 4 mg intraoperatively and on postoperative day one had reduced nausea and vomiting and improved appetite after surgery. A prospective, randomized, placebo controlled study is being conducted to investigate the effects of low dose dexamethasone on serum cytokines and quality of recovery following CPB.

METHODS: Preliminary post operative nausea and vomiting results from the first 66 of 120 patients are being reported. After providing IRB-approved written informed consent, 66 patients were randomized to receive dexamethasone or placebo. All patients were scheduled to undergo elective primary CABG or primary single valve repair/replacement. Exclusion criteria included: combined CABG/valve; EF < 30%; preoperative inotropic agents or IABP; use of preoperative steroids; preoperative mechanical ventilation; renal failure; and emergency surgery. The dexamethasone group received 8 mg of dexamethasone at induction of anesthesia and an additional 8 mg on initiation of CPB. Patients completed a questionnaire assessing nausea and vomiting at baseline preoperatively, on postoperative day #1, and postoperative day #2 in addition to the QoR-40. Fischer's exact test was used to compare the incidence of nausea and vomiting between groups at each time point.

RESULTS: Interim analysis shows no significant difference between the placebo and dexamethasone groups at any time points.

DISCUSSION: Only one prior study has investigated the use of low dose dexamethasone in recovery following cardiac surgery. In their study of 300 patients they found that dexamethasone (4mg) given at induction of anesthesia and additionally on postoperative day 1 was useful in reducing emetic symptoms compared to placebo. Our interim analysis did not replicate their findings which may be attributed to sample size as well as timing of dexamethasone administration.

CONCLUSION: Interim analysis reveals that low dose dexamethasone administered at induction of anesthesia and on initiation of CPB does not decrease the incidence of postoperative nausea and vomiting following cardiac surgery.

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LOW DOSE DEXAMETHASONE DOES NOT INCREASE PERIOPERATIVE HYPERGLYCEMIA IN PATIENTS UNDERGOING UNCOMPLICATED CARDIAC SURGERY

Patel K; Sherwani S; Lin L; Gupta D; Murphy G

Northshore University Health System; Northwestern Memorial Hospital

INTRODUCTION: Low dose dexamethasone is well known to improve quality of recovery following non cardiac surgery. In cardiac surgery, there have been several studies showing unfavorable outcomes associated with postoperative hyperglycemia. There are no large scale, randomized, placebo controlled studies associating an increase in hyperglycemia with low dose dexamethasone therapy. A prospective, randomized, placebo controlled study is being conducted to investigate the effects of low dose dexamethasone on serum cytokines and quality of recovery following CPB.

METHODS: Preliminary results of perioperative glucose levels from the first 66 of 120 patients are being reported. After IRB-approved written informed consent, 66 patients were randomized to receive dexamethasone or placebo. Patients underwent primary CABG or primary single valve repair/replacement. Exclusion criteria included: combined CABG/valve; EF < 30%; preop inotropic agents or IABP; preop steroid use; preop mechanical ventilation; renal failure; and emergency surgery. The dexamethasone group received 8 mg of dexamethasone at induction of anesthesia and an additional 8 mg on initiation of CPB. Glucose levels are measured at four time intervals: baseline at induction of anesthesia, 15 minutes after separation from cardiopulmonary bypass, on admission to the intensive care unit, and 30 minutes after tracheal extubation. Intraoperatively, patients were treated in accordance with the Portland Protocol to maintain glucose levels < 250 mg/dL. Postoperatively, all patients were placed on an insulin infusion to maintain glucose levels 80-110 mg/dL. Differences in glucose between time points and treatment groups were isolated using a two-factor repeated measures ANOVA with post-hoc Dunnet's test ($p < 0.05$).

RESULTS: Interim analysis shows that there is no statistically significant effect of dexamethasone on glucose at all measured time points. Glucose measurements are significantly higher than baseline immediately post-CPB. However, there is no intergroup difference in glucose levels immediately post-CPB.

DISCUSSION: Hyperglycemia has been shown to lead to unfavorable outcomes following cardiac surgery. Previous high dose dexamethasone studies in cardiac surgery have been shown to cause hyperglycemia in this subset of patients. There has been concern that even low dose dexamethasone may cause hyperglycemia in cardiac surgery patients. However, our interim analysis shows that this is not the case. Glucose levels in both placebo and dexamethasone treatment groups closely mirror each other.

CONCLUSION: Interim analysis reveals that low dose dexamethasone administered at induction of anesthesia and on initiation of CPB does not cause a significant difference in glucose levels at all measured time points post-CPB.

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MAJOR PERIOPERATIVE ADVERSE EVENTS FOLLOWING CARDIAC SURGERY IN PATIENTS WITH IMPAIRED GLUCOSE TOLERANCE

Subramaniam B; Gerstle J; Jidge S; Mahmood F; Lerner A; Khabbaz K; J P

Beth Israel Deaconess Medical Center

Background: Patients with undiagnosed Diabetes Mellitus or impaired glucose tolerance may have increased incidence of major perioperative adverse events such as myocardial infarction, renal failure, stroke and death. **Methods:** Patients with index cardiac surgery from Jan 2008 to August 2009 were tested for HbA1C on the day or within 2 weeks prior to surgery after IRB approval. 927 (83%) patients had preoperative HbA1C drawn and 69% of these patients were non-diabetics. Although, currently HbA1C is not used as a screening tool for diagnosing diabetes, a HbA1C <6% was used to define true non diabetics and HbA1C \geq 6% was used to define impaired glucose tolerance. The primary outcome was a composite of postoperative stroke, myocardial infarction, renal failure and death per Society of Thoracic Surgery (STS) definitions. The confounders for HbA1C were identified. The covariates for the logistic regression based on the outcomes and confounding were chosen with a $p < 0.25$ and scientific plausibility. A backward regression method was used and HbA1C was forced into the final model. SAS version 14.0 (Chicago, IL) was used for statistical analysis. $P < 0.05$ was considered significant. **Results:** Patients in the impaired glucose tolerance group had HbA1C values from 6 to 7.8% (mean 6.2) and a higher incidence of significant comorbidity (Table 1). The perioperative outcomes were not significantly different between the two groups as shown in Table 1. The characteristics between patients with and without outcomes is shown in Table 2. Age, STSmorbiditymortality score, type of surgery, preoperative congestive heart failure, body surface area, hypertension and crossclamp time were chosen for the model. The final model had Cross clamp time ($p=0.025$, OR=1.011, CI 1.001 to 1.021 for every min increase), History of CHF ($p=0.075$, OR=0.51, CI 0.24-1.1) and HbA1C(6or more Vs 6)($p=0.61$, OR=0.83, CI 0.39-1.7)as significant risk factors.

Conclusion:

Patients with impaired glucose tolerance have similar perioperative outcomes compared to the non diabetics with HbA1C <6. It is also possible that impaired glucose tolerance may not be defined with a HbA1C cutoff of 6.

MITOCHONDRIAL GENOMIC VARIATION ASSOCIATED WITH INCREASED RATES OF PERIOPERATIVE MYOCARDIAL INFARCTION FOLLOWING CARDIAC SURGERY

Lobato R; Dobson S; Mathew J; Newman M; Podgoreanu M

Duke University

Background: The mitochondrial genome contains 37 genes encoding for critical subunits of the electron transport chain. Sequence variants in mitochondrial DNA (mtDNA) have been implicated in a variety of diseases caused by abnormal ATP production, apoptosis, or reactive oxygen species (ROS) toxicity[1]. Despite this, the role of mitochondrial genomic variation in modulating myocardial responses to planned ischemia-reperfusion and perioperative stress associated with cardiac surgery has not been characterized. We tested the hypothesis that specific single nucleotide polymorphisms (SNPs) in mtDNA are associated with the incidence of perioperative myocardial infarction (PMI) in cardiac surgical patients.

Methods: With IRB approval a prospective cohort of 644 patients undergoing elective cardiac surgery with cardiopulmonary bypass was enrolled at a single institution. We genotyped 138 mtDNA tagging SNPs using the Human 610-Quad bead chip (Illumina Inc., San Diego CA). No heteroplasmy (detected as heterozygous samples) was observed. Serial perioperative plasma levels of creatine kinase-MB (CK-MB) were measured by immunoassay (Siemens, upper limit of normal 5ng/ml). PMI was defined as CK-MB>50ng/ml (10xULN) on first two postoperative days. To reduce the number of potential mitochondrial haplogroups, only patients of self-identified European ancestry were included in the analysis. Mitochondrial SNPs with minor allele frequencies >5% were tested for association with PMI using Pearson Chi-squared tests. Unadjusted and Bonferroni-adjusted p-values were calculated for each association test performed.

Results: Genotypic and phenotypic data were available for 633 patients in the cohort. Of the 138 mitochondrial SNPs represented on the 610-Quad chip, 25 SNPs had minor allele frequencies >5%. PMI was diagnosed in 112 individuals (17.7% of the cohort). We found significant evidence for association between a mitochondrial SNP located within the ND2 gene and increased incidence of PMI ($p=0.002$, Figure). The association remained significant after adjustment for multiple comparisons ($p=0.036$) and conferred an odds ratio of 2.44 (1.39, 4.29).

Discussion: We provide novel evidence for an association between a non-synonymous polymorphism in the NADH dehydrogenase subunit 2 (ND2) of mitochondrial electron chain (Complex I) and increased risk of PMI. Proposed mechanistic consequences of this substitution include increased ROS production and less efficient Complex I function [2]. Carriers of the ND2 polymorphism may have a reduced ability to respond to the oxidative challenges associated with myocardial ischemia-reperfusion and subsequent high-energy demand physiological states that accompany cardiac surgery.

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MITRAL VALVE GEOMETRIC CHANGES AFTER AORTIC VALVE REPLACEMENT

Fritsch M; Chaudhary B; Mahmood F; Chaudhary H; Subramaniam B; Panzica P; Karthik S; Mahmood F

Albany Medical School; Beth Israel Deaconess Medical Center

OBJECTIVE: We sought to evaluate whether geometric changes occur to the mitral valve after aortic valve replacement (AVR).

BACKGROUND: Even with the improved ability to evaluate the mitral valve using 3-dimensional transesophageal echocardiography, changes in mitral valve geometry immediately after aortic valve replacement has not been evaluated. The fibrous structure of the heart includes both the mitral and aortic valves, which are situated in close proximity. It is possible that surgical manipulation of one these valves, especially valve replacement with a prosthesis, would alter the geometry of the other native valve. This study was designed to determine if geometric changes occurred to the mitral valve after AVR and to quantify those changes.

METHODS: This is an ongoing study evaluating twenty patients undergoing AVR or a combined coronary revascularization and AVR procedure. The patients had both pre- cardiopulmonary bypass (CPB) and post- CPB transesophageal echocardiography exams including live 3-D mitral valve assessment. Data from both the pre- and post- CPB mitral valve assessments were analyzed offline using the TomTec 3D mitral valve analysis program. The various geometric measures at end-systole included: antero-posterior (AP) diameter, anterolateral-posteromedial diameter, posterior and anterior annulus lengths, annular area, annular circumference, non-planarity angle, and sphericity index.

RESULTS: Preliminary data from a portion of the study subjects demonstrate that significant shape changes to the mitral valve occur after AVR. Although there was no significant difference in AP diameter, AL-PM diameter, annulus area or circumference, there was a significant difference in the non-planarity angle and sphericity index post-AVR. Non-planarity angle increased from 149 degrees to 155 degrees and sphericity index increased from 0.73 to 0.84.

CONCLUSIONS: Preliminary data from this ongoing study suggests that a shape change does occur to the mitral valve after AVR. The data demonstrates that the mitral valve becomes flatter and more circular after AVR.

NEUROIMAGING AND CLINICAL MANIFESTATIONS OF ORGANIC BRAIN INJURY AFTER CARDIAC SURGERY

Saha C; Lee C; Katznelson R; Jerath A; Fedorko L; Carroll J; Djaiani G

TGH

Introduction: Cumulative neuroimaging and clinical correlation evidence indicates that ischemic brain injury is responsible for the development of global neurological deficit after cardiac surgery. The objective of this study was to determine relationship between postoperative neuroimaging findings and clinical manifestations of neurological complications in patients undergoing cardiac surgery.

Methods: Following REB approval we reviewed clinical and neuroimaging data collected prospectively from June 2008 to May 2009 of patients undergoing cardiac surgery with cardiopulmonary bypass (CPB). Patients underwent either brain diffusion weighted magnetic resonance imaging (DW-MRI) or computed tomography (CT) scanning. Indications for postoperative neuroimaging included presence of neurological deficit, delirium, clinical seizures, and decreased level of consciousness. Based on neuroimaging findings patients were classed into three groups; new brain infarcts, old brain infarcts, and controls (normal scan). All patients were assessed for delirium postoperatively daily for 5 days using the Confusion Assessment Method in Intensive Care Unit (CAM-ICU). Patients who were CAM-ICU 'positive' were examined by a psychiatrist to confirm the diagnosis of delirium. Neurological examination was conducted daily by the attending anesthesiologist. Data expressed either as mean \pm SD, or number of patients (%).

Results: A total of 17 (16%) and 89 (84%) patients underwent DW-MRI and CT scanning respectively. CT scanning was repeated within a 3-4days interval if the primary scan was negative for organic brain injury. 25 (23.5%) and 38 (36%) of patients were found to have new and old brain infarcts respectively. (Table) Delirium was present in 77 (72%), seizures in 36 (34%), and clinically manifested perioperative stroke in 18 (17%) patients. All seizures occurred within 10 hours of surgery. Seizures were more likely to occur in patients without brain infarcts. Delirium rates were similar in patients with or without brain infarcts.

Conclusions: Organic brain injury after cardiac surgery with CPB is relatively common. Delirium and seizures are not associated with either acute or chronic brain injury.

ONE INSTITUTION'S INITIAL EXPERIENCE WITH TECAB SURGERY

Dhawan R; Roberts J; Chaney M

University of Chicago

Introduction: The first Totally Endoscopic Coronary Artery Bypass (TECAB) procedure was performed in 1998 yet the clinical application of the technique remains somewhat controversial (1-3). Potential advantages include less postoperative pain and a quicker postoperative recovery. Potential disadvantages include unique intraoperative technical challenges that may lead to increased postoperative morbidity. We report here our Institution's initial experience with TECAB surgery.

Methods: Following IRB approval, we retrospectively reviewed the medical records (anesthetic/surgical/postoperative) of our Institution's first 25 patients undergoing TECAB (NOV 2007-MAR 2008). One experienced surgeon performed every TECAB. Patient demographic data (Euroscore calculated), number of grafts performed, length of ICU/hospital stay, and associated morbidity/mortality were assessed.

Results: Mean patient age was 63.4 years (range 44-84) and 36% were female. Mean Euroscore calculation (4) was 3.47% (range 0.88-6.85). Mean number of distal grafts was 1.76 (range 1-3). Mean duration of surgery was 4.9 hours, mean duration of operating room time was 7 hours, and mean intraoperative one-lung ventilation time was 3.8 hours. Two patients did not tolerate intraoperative lung separation and required two-lung ventilation during TECAB. Two intraoperative conversions to a thoracotomy approach were required due to hemodynamic instability. Mean ICU length of stay was 2.7 days (range 1-22), and mean hospital length of stay was 5.2 days (range 2-24). Of our initial 25 patients, there was no mortality yet two patients experienced substantial morbidity. One patient (72 yr old female) experienced intraoperative cardiac arrest requiring thoracotomy and emergent initiation of fem-fem CPB (subsequent anoxic brain injury). The next postoperative day this patient returned to the operating room for repair of a leaking graft anastomosis through a sternotomy approach. The other patient (49 yr old female) underwent uneventful initial TECAB (discharged home on third postoperative day) however she presented two months later with graft failure and ischemic myocardium requiring emergent cardiac catheterization and stent placement.

Conclusion: The clinical advantages and disadvantages of Robotic TECAB surgery remain controversial (1-3). Our Institution's initial TECAB experience reveals that mean postoperative length of stay (ICU/hospital) was acceptably low. However, our initial experience also indicates potential intraoperative challenges such as prolonged surgical/operating room/one-lung ventilation times and conversion to thoracotomy. Furthermore, intraoperative hemodynamic instability seemed to be unexpectedly common (one patient required emergent initiation of CPB). Lastly, short-term and long-term graft patency associated with Robotic TECAB revascularization remains questionable.

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PAIN LEVELS AFTER MINIMALLY INVASIVE CARDIAC SURGERY: RESULTS FOR THE FIRST 7 DAYS

Lebon J; Rochon A; Ayoub C; Deschamps A; Bouchard D; Qizilbash B; Couture P; Denault A; Belisle S; Hemmings G; Toledano K; Taillefer J; Blain R; Cogan J

Montreal Heart Institute, Université de Montréal

Background:

Minimally invasive cardiac surgery (MICS) is thought to be less painful and lead to an easier and earlier recovery than open sternotomy. We report here on 101 consecutive patients who have undergone MICS at the Montreal Heart Institute (MHI) since February 2007 .

Aims: to describe the “average” postoperative pain with movement.

Methods:

After ethics approval all patients undergoing MICS were followed at 24 hours, 48 hours, and 7 days post surgery. We collected information on pain intensity and site of pain at every visit and, additionally, on day 7 we collected information related to barriers to taking pain medication and degree of satisfaction with care.

Results

One hundred and one patients have been followed to date; the mean age is 56.8 years and 59% were male. Average pain levels on movement at 24 hours, 48 hours and 7 days were 5.3, 5.2 and 3.9 respectively. The percentage of patients with average pain on movement greater or equal to 4 on the NRS at 24 hours, 48 hours and 7 days were 74%, 77.5% and 56.5%, respectively. The most common secondary effects at 48 hours were dry mouth 78%, sleepiness and fatigue 68% and nausea and dizziness 57%. At 7 days the most common secondary effects were fatigue 78%, dry mouth 60% sleepiness 49% and dizziness 47%. Although overall satisfaction with care was very high at 89%, only 5 patients stated that a nurse had provided instructions regarding the importance of good pain management and only 3 patients stated that a nurse explained the importance of letting medical staff know if he/she was in pain.

Conclusion

These pain scores do not differ from pain scores obtained in our hospital in February 2009 for patients undergoing open sternotomy. Average pain on movement after open sternotomy was 5.47 at 24 hours, 5.45 at 48 hours, and 4.33 on day 5. These data and the significant amount of secondary effects suggest that Minimally Invasive Cardiac Surgery does not appear to be as pain free as was originally postulated. This may be related to the intercostal insertion of scopes, instruments and post surgical drains which disrupt nerve endings, muscle and cartilage in an area known for its high potential for postoperative pain.

PATIENTS ARE NOT NORMOVOLLEMIC FOLLOWING CARDIAC SURGERY DESPITE CONCERTED EFFORTS TO MANAGE FLUID AND VOLUME STATUS

Nelson M; Bruce S; Reddy P; Kearney J; Green J; Nicolato P; Brinster D; Kasirajan V

Virginia Commonwealth University

Purpose

Following cardiac surgery, fluid replacement therapy is employed to maintain patients in a normovolemic state. Standard surrogate measures of volume status are used as guides in volume assessment and restoration. Direct blood volume measurement was utilized to determine the patients' true volume status .

Methods

Three blood volume measurements were performed on each of 36 patients: (1) before surgery; (2) immediately following surgery; and (3) 2 hours after transfer to the ICU. Total Blood Volume (TBV), Red Blood Cell Volume (RBCV) and Plasma Volume (PV) were measured using the indicator dilution technique via a commercially available, FDA approved semi-automated system (BVA-100 Blood Volume Analyzer, Daxor Corporation).

Results

Blood volume analysis revealed that the majority of patients 25/36 (69.4%) entered surgery in a hypervolemic state. Following surgery, 19/36 (52.8%) of patients had become hypovolemic – despite the fact that commonly used invasive technology indicated that they were normovolemic.

Conclusions

Blood volume analysis provided direct measurement of the volume status of patients before and after cardiac surgery for the first time. Although all patients were believed to be euvolemic following surgery, direct blood volume measurement revealed that the majority of patients were in fact volume expanded prior to surgery and volume contracted after surgery. We postulate that the use of vasoconstrictors, hypothermia, and avoidance of volume overload in post-operative patients are potential mechanisms which may contribute to the large degree of hypovolemia observed in post-operative patients.

PERIOPERATIVE ASSESSMENT OF RIGHT VENTRICULAR STROKE VOLUME USING 3D TRANSESOPHAGEAL ECHOCARDIOGRAPHY.

Karhausen J; Phillips-Bute B; Swaminathan M; Mackensen G; Mathew J

Duke University; Duke University Medical Center

Background: Perioperative echocardiographic evidence of right ventricular (RV) dysfunction has been associated with poor outcome both in valvular and coronary artery bypass grafting surgery. However, the functional assessment of the right heart remains problematic, as the geometric complexity of this crescent-shaped chamber does not lend itself well to two-dimensional imaging. Indices of RV performance seem to provide clinically relevant information but remain conceptually difficult and lack information on regional wall motion. The recent introduction of 3-dimensional transesophageal echocardiography (3D-TEE) has provided clinicians with a new tool to assess RV geometry and function. This study aimed to a) evaluate the utility of 3D-TEE data and built-in quantification software to reproducibly measure RV stroke volume (RVSV) and b) correlate RVSV to left ventricular stroke volume (LVSV) in the perioperative setting.

Methods: With IRB approval, 3D-TEE full volume loops from 34 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 Healthcare, MA). Digitized images were assessed off-line by independent investigators for right and left ventricle using built-in software (QLAB 7.0, Philips Healthcare, MA). End-diastolic (EDV), end-systolic (ESV) ventricular volumes and resultant stroke volumes were noted for each ventricle. Coexisting valvular disease was determined echocardiographically and graded according to current ASE/SCA guidelines. Pearson correlation was used to assess correlation between RVSV and LVSV.

Results: Mean LVSV measured 55.5 ml (21.5-115.5 ml) while mean RVSV was 50.3 ml (18.4-135.1 ml). Pearson correlation between these measurements was $r=0.54$ for the whole sample (Fig. 1A, black dotted line shows observed correlation). In the subset of patients with no more than mild valvular disease ($n=18$) correlation was markedly improved with $r=0.74$ (Fig. 1B).

Conclusion: This study provides preliminary evidence that 3D-TEE RV stroke volume assessments adequately correlate with established 3D-TEE quantification of left ventricular stroke volume. Correlation between right and left ventricular stroke volumes has been previously confirmed with other imaging modalities (1). As assumed on the basis of the continuity principle, such correlation is markedly weakened in the presence of significant valvular abnormalities. While this study used software not specifically designed for the geometrical configuration of the right ventricle, the data nevertheless suggest that RV volumes may be reproducibly measured with 3D-TEE.

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PERI-OPERATIVE RISK AND ANESTHETIC MANAGEMENT OF PATIENTS WITH EXTREME HYPERTENSION

Culp, Jr. W; Spatz T; Patel V; Ball T; Bohannon W

The Texas A&M University System Health Sciences Center College of Medicine; The Texas A&M University System Health Sciences Center College of Medicine, Scott & White Memorial Hospital

Background

Patients with poorly controlled hypertension have historically had a high perioperative complication rate and are often deferred for surgery until better controlled. While hypertensive patients reportedly experience intraoperative blood pressure (BP) lability, there is little current data on the perioperative risk faced by patients with extreme hypertension. We sought to assess perioperative complications and BP lability in this high-risk group by evaluating severely hypertensive patients refractory to anti-hypertensive agents who underwent general anesthesia for a surgical procedure.

Methods

Fourteen patients with resistant, stage II hypertension who received general anesthesia were evaluated in this IRB-approved study. The procedure involved a standard induction and inhalational anesthetic using isoflurane, followed by a total intravenous anesthetic (TIVA), and then concluded with an inhalational anesthetic. Intraoperative BP was analyzed, along with any evidence of acute myocardial infarction (AMI), stroke, renal failure, death, or other complication within 30 days of operation. BP values were from an automated anesthetic record.

Results

Of the 14 patients, the average pre-operative BP was $186\pm 19/108\pm 17$ mmHg, average age 53 ± 11 years, 10 were men. One had an asymptomatic creatinine rise from 0.95 mg/dL to 1.60 mg/dL (68% increase) one hour postoperatively, which resolved spontaneously within 48 hours. One patient with prior history of AMI had a transient troponin rise post-operatively without EKG changes or symptoms and later underwent coronary re-vascularization. One patient suffered some facial weakness and dysarthria 11 days post-operatively that resolved spontaneously. No other complications were noted. Mean arterial blood pressure (MAP) lability is summarized in Figure 1. No significant MAP differences are noted between inhalational and TIVA anesthetics.

Conclusions

Intraoperative hypotension likely led to the mild renal injury seen in one subject, consistent with the 8% predicted incidence of this complication. One subject who had a troponin elevation (though did not meet criteria for AMI) may not have had this chemical marker elevation had revascularization been performed pre-operatively. Charleson found an 8% risk of MI or cardiac arrest in patients with extreme hypertension undergoing noncardiac surgery, consistent with our data.¹ Our BP changes data demonstrate that in the extreme hypertension population, further BP elevations are unlikely, however hypotension is frequent and often refractory to standard vasoconstrictor dosing, requiring more aggressive therapy to maintain BP. Type of anesthetic (inhalational versus TIVA) made no substantial difference in the BP lability. We suspect that achieving BP within 10-20% of baseline may reduce the incidence of renal failure. Further studies examining larger samples will allow more accurate risk assessment for this high risk population.

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PERIOPERATIVE SERUM CREATININE LEVELS ARE A SENSITIVE PREDICTOR OF MORTALITY IN PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFT SURGERY WITH CARDIOPULMONARY BYPASS

Pan W; Tolpin D; Lee V; D C; Elayda M

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

Introduction: Lassnigg et al. previously reported that a postoperative change of serum creatinine level independently predicted mortality in patients undergoing cardiothoracic surgery. However, this study did not control for preoperative renal function, and was potentially confounded by inclusion of multiple types of cardiothoracic surgeries. Using a retrospective cohort (n=4135) of patients undergoing primary coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass (CPB) at a single institution between January 2002 and December 2007, we investigated whether a postoperative change of creatinine level (Δ creatinine) independently predicts 30-day all-cause mortality in patients with normal and abnormal preoperative renal function (RF).

Methods: Patients were classified into four groups according to their preoperative glomerular filtration rates (GFR): normal RF (GFR \geq 90 ml/min per 1.73 m²; n=1119), mild renal insufficiency (RI)(GFR 60 - 89 ml/min per 1.73 m²; n=1937), moderate RI(GFR 30 - 59 ml/min per 1.73 m² ; n=895), and severe RI (GFR < 30 ml/min per 1.73 m²; n=184). Patients requiring preoperative dialysis were excluded. GFR was estimated using the Modification of Diet in Renal Disease study equation. Multivariate logistic regression was performed, controlling for patient demographics, medical history and preoperative medications, to determine if Δ creatinine was associated with 30-day all cause mortality. Δ creatinine was defined as the difference between postoperative (within first 48 hr) and preoperative serum creatinine levels.

Results: Δ creatinine was independently associated with 30-day all-cause mortality in patients with preoperative normal RF (OR=6.83; 95% CI=2.81 to 16.63; P<0.01), mild RI (OR=16.29; 95% CI=7.60 to 35.95; P<0.01) and moderate RI (OR=2.59; 95% CI=1.60 to 4.18; P <0.05), but not severe RI. Additionally, mortality was directly related to Δ creatinine, and exponentially higher when Δ creatinine \geq 0.5 mg/dl. Postoperative mortality was lowest in patients with a decreased serum creatinine level of 0.1 mg/dl: 0.4% in preoperative normal RF, 0.7% in mild RI, and 0.9% in moderate RI. Mortality was significantly higher in patients with no change in serum creatinine as compared to patients with a Δ creatinine = -0.1 mg/dl (P <0.05). Figure 1 shows mortality in each Δ creatinine group and result of multivariate regression analysis in a combined group of all patients with normal RF, mild RI, and moderate RI.

Conclusion: In patients with preoperative normal RF, mild and moderate RI, Δ creatinine is an independent and sensitive predictor of postoperative mortality in patients undergoing CABG surgery with CPB.

PHARMACOKINETICS OF AMINOCAPROIC ACID IN NEONATES

Eaton M; Haas C; Dawn S; Ronald A; Cholette J

University of Rochester

Background: Epsilon Aminocaproic Acid is a lysine analogue anti-fibrinolytic drug that has been shown to be effective in reducing bleeding and transfusion associated with cardiac surgery involving cardiopulmonary bypass (CPB) in adults [1] and children[2]. Most studies have used empiric dosing, but recently the kinetics of EACA in adults have been explored and published.[3] Ririe et al, have described the kinetics of EACA in older infants and children up to the age of four years[4] which were significantly different compared with adults. Neonates have significantly different pharmacokinetic and pharmacodynamic parameters than adults and older children [5] and represent a large proportion of patients undergoing congenital heart surgery. The kinetics of EACA in neonates undergoing cardiac surgery are unknown.

Methods: After IRB approval and informed parental permission, ten neonates less than 1 month of age presenting for elective cardiac surgery with CPB were enrolled. To ensure 95% of patients would be above the established therapeutic concentration of 130 mcg[6], a concentration of 260 mcg/ml was targeted. Patients were given a loading dose of EACA, 75 mg/kg over ten minutes starting during surgical skin preparation, and an infusion of 75mg/kg/hr until protamine administration. 25 mg of EACA were added to the prime volume of the CPB pump for each 100 ml of prime volume.

Blood samples for EACA concentration were drawn at the following times: (1)Immediately prior to EACA administration, (2)3 minutes after the bolus was completed, (3) immediately prior to the initiation of CPB, (4)5 minutes after starting CPB, (5)1 hr after starting CPB, (6)immediately before weaning from CPB, (7)immediately before stopping the infusion, and (8)30, (9)90 and (10)180 minutes after stopping the infusion. EACA levels were evaluated using gas chromatography/mass spectroscopy.

Results: Although there was a large amount of between patient variability, the dosing scheme established and maintained effective concentrations in all patients for every specimen but two during CPB. (see Fig.) Mean concentrations for the three sampling times during CPB were 262.4, 267.5, and 262.2.

Discussion: The dosing scheme we used, as adapted from Ririe, et al, established and maintained effective concentrations of EACA in essentially all neonates. There was a large degree of inter-subject variability. Kinetic modeling is underway to further describe neonatal distribution and elimination of EACA.

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POTENTIAL ROLE OF STATIN PLEIOTROPY IN THE NGAL/CREATININE RELATIONSHIP FOLLOWING CARDIAC SURGERY

Heerdt P; Heerdt P; Wagner C; Chan J; Fontes M

Weill Cornell Medical Center; Weill Cornell Medical College

Studies suggest an association between postoperative threshold urine or plasma values for neutrophil gelatinase-associated lipocalin (NGAL) and clinically significant acute kidney injury (AKI) manifest as pre-defined increases in plasma creatinine (1,2). These data, however, tend to exhibit substantial overlap of NGAL values between patients with and without AKI, reflecting the fact that AKI is generally categorized as an all or none phenomenon. Furthermore, the pathogenesis of postoperative AKI is multifactorial reflecting not only the intraoperative insult but also pre-existing subclinical dysfunction and possibly pharmacotherapy. Recent reports indicate that statin therapy may have generalized renal protective effects due to anti-inflammatory and/or antioxidant actions (3). We hypothesized that when plotted as continuous variables, the correlation between the postoperative rise in plasma NGAL and the maximal rise in creatinine over the first 48 hours will be altered by statin therapy. Methods: Data from 61 cardiac surgical patients were reviewed for the study. For each patient, NGAL and creatinine were measured in blood samples obtained preoperatively, upon admission to the ICU, and on the first postoperative day (POD1). Creatinine was also measured in an additional sample obtained on postoperative day 2. From this data set, two groups (statin or no statin) of 16 patients matched for age, gender, preoperative creatinine and duration of CPB were selected. The peak change in serum creatinine relative to baseline over the first 48 hours for each patient was then plotted as a function of the change in NGAL upon ICU admission and on POD1, and analyzed by linear regression..

Results: As shown in figure 1, pre- and postoperative NGAL levels were the same in both the statin and no statin groups. However, as shown in figure 2, for the no statin group, there was close correlation between the peak change in creatinine over 48 hours and the change in NGAL both upon ICU admission and on POD1. No such correlation was present for the statin group at either time point.

Conclusions: Although the absolute increases in NGAL were the same for both statin and no statin groups, the data demonstrate a relationship between postoperative changes in NGAL and creatinine only in patients not treated with a statin. These findings suggest that statin pleiotropy may modify some of the factors modulating the impact of cardiac surgery with CPB on the kidney.

References

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PREDICTORS OF COGNITIVE RECOVERY AFTER CARDIAC SURGERY

Swift R; Phillips-Bute B; Podgoreanu M; Stafford-Smith M; Newman M; Mathew J

Duke University Medical Center

Introduction: Neurocognitive decline occurs frequently in the elderly after cardiac surgery, and persists in an important percentage of patients. While predictors of cognitive injury have been well studied, factors that modulate cognitive recovery have not been examined. We therefore sought to determine the predictors of cognitive recovery after initial injury following cardiac surgery.

Methods: After IRB approval, 1477 patients undergoing CABG, Valve, or CABG + Valve surgery with cardiopulmonary bypass and who had enrolled in a cognitive outcomes trial were retrospectively evaluated. Patients were excluded from the cognitive trial if they had a history of symptomatic cerebrovascular disease, psychiatric illness, creatinine >2 mg/dL, <7th grade education, or had a Mini Mental State Examination score <24. Patients in these trials were evaluated with a well-validated battery of 5 cognitive tests at baseline, 6 weeks, and one year after surgery. Test scores were subjected to factor analysis to calculate the cognitive index (mean of the 4 domain scores; CI), a continuous measure of cognitive function. 749 patients showed a decline in CI from baseline to 6 weeks; of these, 229 had complete data at all three time points. These patients were considered "decliners" and were included in the analysis dataset. Cognitive recovery was defined as 1-year CI \geq baseline CI. Potential predictors of cognitive recovery including patient characteristics, quality of life factors, comorbidities, medications, and intraoperative variables were assessed univariately and then with multivariable regression modeling; $p < 0.05$ was considered significant.

Results: Of the 229 patients, 178 underwent CABG surgery, 32 had CABG + valve surgery, and 19 had valve surgery. 103 patients (45%) experienced cognitive recovery while 126 (55%) remained below baseline. There were no significant differences between those who recovered and those who did not with regard to age, gender, comorbidities (diabetes, hypertension, COPD, post-op atrial fibrillation or renal insufficiency, Euroscore), medications (statins), depression, anxiety, marital status, or level of social support. Multivariable analyses revealed years of education ($p < 0.001$), baseline cognitive index ($p = 0.02$), amount of cognitive decline at 6 weeks ($p = 0.004$), and the 6 week activities of daily living (IADL) score ($p = 0.02$) as significant predictors of cognitive recovery (Figure 1; higher IADL scores are worse).

Conclusions: Cognitive recovery at 1-year occurs in approximately one half of the patients experiencing injury at 6 weeks after cardiac surgery. Of note, age, depression, and social support systems do not appear to modulate this recovery. The association between cognitive recovery and increased activities of daily living at 6 weeks suggests that efforts to promote early physical and mental exercise after surgery may be beneficial.

PREDICTORS OF HEPARIN RESISTANCE IN AN INTERNATIONAL COHORT OF CARDIAC SURGICAL PATIENTS

Fontes M; Lee K; Suh A; Skubas N; Miao Y; Mangano D

Ischemia Research and Education Foundation; Weill Medical College of Cornell University

Introduction: Endothelial disruption associated with atherosclerotic plaques and pulsatile injury associated with both systolic hypertension (ISH) and widened pulse pressure (PP) may contribute to a subclinical prothrombotic state involving activation of the coagulation/tissue factor and platelet pathways with thrombin generation. As such, we hypothesize that heparin resistance (HR) is more common in these patients due to a reduced level of antithrombin III.

Methodology: Following IRB approval, we conducted a prospective observational study involving 5,436 patients having elective CABG surgery requiring cardiopulmonary bypass (CPB). Of these, 5,065 met final inclusion criteria. Comprehensive data were captured for past medical history, hemodynamics, perioperative medications and laboratory measures, coagulation profile and post-CPB haemostatic events. Primary outcome was HR defined as an ACT value of <480 seconds after the initial dose of heparin. Secondary outcomes included: >2 doses of heparin to achieve adequate ACT before CPB, intraoperative clinical diagnosis of HR and post-CPB severe coagulopathy. Up to 40 predictor variables were tested by univariate analysis; those with a p value of <0.2 were subsequently entered into a multivariate model to determine independent predictors of HR. Significance was set at p <0.5.

Results: The primary outcome of HR was observed in nearly ¼ of patients. Thirteen % required > 2 doses of heparin to achieve acceptable pre CPB ACT; 4.92% had an intraoperative clinical diagnosis of HR; and 1.94% experience severe coagulopathy. Both ISH and PP were predictors of HR by univariate analysis; however, only PP remained an independent predictor by multivariate analysis along with Euro SCORE, preoperative heparin therapy, minimum hemoglobin (Hgb), minimum platelets and intraoperative antifibrinolytics. Independent predictors of >2 doses of initial heparin are shown in Table 1. For clinical diagnosis of HR, the following predictors were also identified: preoperative heparin, minimum hemoglobin, minimum platelets, lowest ACT prior to CPB and antifibrinolytics. Lastly, CPB time was the sole independent predictor of severe coagulopathy.

Conclusion: Failure to achieve an ACT value of >480 seconds is common and significantly associated with widened PP, severity of preoperative morbid state, heparin therapy, Hgb, platelets and antifibrinolytic medications. Further studies are necessary to address the specific haemostatic abnormality present in individuals with high PP and the interaction between antifibrinolytics and ACT measurement.

PREOPERATIVE TRANSESOPHAGEAL ECHOCARDIOGRAPHY IN PATIENTS UNDERGOING INTERVENTIONAL ELECTROPHYSIOLOGY PROCEDURES

Keyes Eto J; Mahajan A; Ho J; Chua J

UCLA

Systemic embolization from intracardiac thrombus poses a substantial risk during interventional electrophysiology procedures. Despite patients being appropriately anticoagulated when indicated, we hypothesize that there is a significant number of patients with new findings of thrombus at the time of their procedure. Imaging studies to detect thrombus have been suggested in patients considered high risk for intracardiac thrombus. We looked at preoperative transesophageal echocardiographs done the same day in 260 consecutive patients presenting for either cardioversion or electrophysiology procedures in the cath lab. We sought to investigate the incidence of intracardiac thrombus in patients presenting for cardioversion or ablation of atrial fibrillation, atrial flutter, supraventricular tachycardia or ventricular tachycardia, and determine whether the finding of a thrombus resulted in a change in the patient's course of management. Furthermore, data was analyzed in an attempt to identify risk factors for having intracardiac thrombi, such as specific types of arrhythmias, ejection fraction, left atrial size, presence of spontaneous echo contrast, anticoagulation status and mitral valve pathology. We found an overall thrombus incidence of 9.2% (24 patients), with the majority being in the left atrium or the left atrial appendage. In patients presenting for interventional electrophysiology studies, the significant incidence of intracardiac thrombus, which can change the course of patient management due to the serious sequelae of systemic embolization, justifies the use of preoperative TEE.

PROTEASE ACTIVATED RECEPTOR-4 POLYMORPHISM ASSOCIATED WITH PLATELET ACTIVATION AND PERIOPERATIVE MYOCARDIAL INJURY

Muehlschlegel J; Perry T; Liu K; Fox A; Collard C; Hartwig J; Shernan S; Hoffmeister K; Body S; Smith S

Baylor College of Medicine; Brigham and Women's Hospital

Introduction

Protease activated receptors (PAR)-1 and -4 expressed on human platelets and endothelium are the principal cell membrane receptors for thrombin-mediated platelet activation. PAR4 knock-out mice have impaired coagulation and are protected from induced mesenteric arteriolar thrombosis due to platelets that are unresponsive to thrombin signaling. Functional genetic variation has been described in the human PAR1 gene (F2R), but not yet in the PAR4 gene (F2RL3). Therefore, we examined the association between PAR4 variants and perioperative myocardial injury (PMI) after coronary artery bypass graft (CABG) surgery. Furthermore, we used flow cytometry to identify possible biologic mechanisms including altered platelet surface receptor expression, platelet count, and platelet response to activation.

Methods

In 1054 Caucasians undergoing CABG surgery, 31 haplotype-tagging single nucleotide polymorphisms (SNPs) within 10,000 base pairs of the F2RL3 gene were genotyped. Cardiac troponin I (cTnI) was measured preoperatively and through the first five postoperative days. After adjusting for clinical covariates of myocardial injury, linear regression was used to test the association between PAR4 variants and PMI, defined by peak postoperative cTnI. Permutation-based empirical p-values were used to adjust for multiple comparisons.

Based on the results of this analysis, we prospectively examined platelet rich plasma of 34 patients (20 wild type, 14 risk allele) homozygous for the SNP with the strongest association (rs773857) using flow cytometry for PAR4 receptor expression and response to activation by specific PAR4 activating peptide (AYPGKF). Platelet activation was evaluated by P-selectin expression, von Willebrand factor (vWF) binding and GPIIb/IIIa activation using the antibody PAC-1.

Results

After adjustment for clinical risk factors, 11 SNPs in strong linkage had an additive association with peak postoperative cTnI (point-wise empirical $P < 0.05$), whereby rs773857 survived multiple comparisons (family-wise empirical $P < 0.01$).

The risk genotype was associated with increased platelet count ($3.0 \times 10^7 \pm 0.8$ vs. 4.1 ± 1.0 ; $P = 0.0016$) and vWF binding (mean fluorescence 6.6 ± 1.3 vs. 8.1 ± 1.3 ; $P = 0.0031$) as well as independently associated with vWF binding after adjusting for age and platelet count ($P = 0.02$) (Figure 1).

Discussion

We have identified a novel independent association between a PAR4 genetic variant and PMI after primary CABG surgery. Importantly, this PMI risk allele is associated with variations in PAR4 receptor signaling or conformation leading to a hyperactive response following PAR4 activation. Furthermore, we have also discovered a novel association of the PAR4 PMI risk allele with increased platelet count.

QUANTIFICATION OF TRICUSPID VALVE GEOMETRY USING REAL TIME 3D TEE

Robinson P; Seres T

University of Colorado

Quantification of tricuspid valve annulus using real time 3D TEE.

Prairie Robinson MD, Tamas Seres MD, PhD

Objective:

There is no tricuspid valve (TV) quantification program in the real time three dimensional transesophageal echocardiography (RT-3D-TEE) software package. The Mitral Valve Quantification (MVQ) software (Philips Medical Systems) was used to compare parameters of normal tricuspid annuluses with those that had tricuspid regurgitation (TR) and underwent repair.

Methods:

Normal TV annuluses of 10 patients undergoing procedures involving cardiopulmonary bypass (CPB) were evaluated and quantified with RT-3D-TEE using full volume images and the MVQ software. Pre- and post-CPB studies were performed on each valve. Normal TV was identified as having trace or no regurgitation using two dimensional imaging with color flow Doppler. Three patients with severe TR scheduled for TV repair were evaluated pre- and post-repair. All valves were repaired with Costgrove Edwards annuloplasty rings. The lateral (septum to free wall) and anterior-posterior (AP) (posterior wall to aorta) diameter, annular circumference, annulus area and height were quantified at end systole.

Results:

The parameters of normal annuluses did not change significantly from the pre- and post-CPB exams (first rows of Table 1 and 2). The remodeling of the TV in cases of severe TR represented significant changes in AP diameter, annular circumference and annulus area when compared to normal valves in the pre-CPB period (Table 1). The circumference, area and height of the annuluses were significantly smaller after repair compared to the normal valve annulus parameters post-CPB (Table2).

Conclusion:

The use of RT-3D-TEE imaging and MVQ software provide detailed information about the tricuspid annulus geometry. The 10 normal valves examined in this study had similar values pre- and post-CPB which suggests that the technique was consistent and there were no significant changes in TV annulus geometry during CPB. The TV annulus area after TV repair was significantly smaller than the normal one. The appropriate TV annulus area after repair needs to be determined in the future. This technique has the potential to accurately examine the tricuspid annulus before and after TV repair.

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QUANTITATIVE ECHOCARDIOGRAPHIC ASSESSMENT OF THE MITRAL VALVE: COMPARING 2D VERSUS 3D AND NOVICE VERSUS EXPERT

McCleish L; Mackensen G; Cobey F; Rivera J; Swaminathan M; Phillips-Bute B

Duke University

Background:

The perioperative evaluation of the mitral valve (MV) and its components influences surgical decisions during MV repair and replacement. Although the MV is routinely assessed with 2D transesophageal echocardiography (2D-TEE), the recent introduction of 3D-TEE and available MV quantification software offer new and more detailed evaluation. However, this software has not yet been validated as an accurate, reliable tool for perioperative use. Therefore, we evaluated inter-observer agreement of 2D and 3D-TEE assessments of anterior mitral valve leaflet (AML) length, each performed by a novice and an experienced echocardiographer. The AML was chosen for its role in helping determine valve size in repair and replacement.

Methods:

With IRB approval, live 3D-TEE Zoom and 2D-TEE MV images from 50 cardiac surgery patients were studied. All patients underwent a comprehensive TEE exam including standard 2D as well as 3D assessment (iE33 system; Philips Healthcare). Using the standard model version of the MV quantification software (MVQ QLAB 7.0, Philips Healthcare, MA), both the novice and the experienced board-certified echocardiographer determined the linear length of the AML based on a 3D model of the MV (figure 1). Observers also made a linear caliper measurement of the AML based on an end-systolic 2D-TEE midesophageal long-axis view. Spearman correlation was used to assess the reliability of ratings between observers, as well as to assess agreement within each observer (2D versus 3D).

Results:

Inter-observer reliability, as assessed with Spearman correlation, was moderate for both 2D ($r=0.52$) and 3D ($r=0.37$) assessments. Agreement of 2D versus 3D assessment was high for both, novice ($r=0.81$) and experienced observer ($r=0.75$). For the novice, mean 2D and 3D length ([SPCHAR(plusmn)]SD) of the AML was 23.8 (4.9mm) and 22.7 (4.7mm) respectively. For the experienced observer, mean 2D and 3D measurements were 26.3 (4.9mm) and 24.7 (4.2mm), respectively.

Conclusion:

Our study shows only moderate agreement of 2D and 3D measurements between observers, which may be due to differences in the level of experience in analyzing echocardiographic images. Of interest, there is a high degree of correlation within each observer's assessments (2D versus 3D), indicating that the 3D quantification software used provides similar accuracy compared to 2D-TEE while allowing for a more detailed quantitative assessment of valvular structures. Of note, mean 2D-TEE AML length was greater than 3D-TEE length. This difference may be due to inadvertent oblique measurement of the AML on 2D-TEE images, which is avoided in the 3D-TEE reconstruction of the MV.

REAL TIME 3 D GUIDED SIZING OF THE ANNULOPLASTY- RING IN MITRAL VALVE REPAIR

Ender J; Eibel S; Gessat M; Haentschel D; Falk V; Mohr F; Mathioudakis D; Jacobs S; Mukherjee C

Heartcenter, University Leipzig

Introduction: In patients undergoing mitral valve (MV) repair implantation of an annuloplasty- ring is essential. Correct sizing of the annuloplasty ring is necessary which is performed by the surgeon under direct vision in the cardioplegic arrested heart. Aim of our study was to investigate the additional value of real time 3D transesophageal echocardiography (RT 3D TEE) guided sizing for predicting the size of the annuloplasty ring in MV repair.

Method: After induction of anesthesia a RT 3D TEE (IE 33, Philips, Netherlands) of the mitral valve was performed in patients undergoing elective MV repair using 3 D zoom as well as full volume mode. These loops were inserted into a modified version of 4D valve assessment® software (Tom Tec Munich, Germany) called ring tool®. This software allows superimposing of computer aided design (CAD) models of real annuloplasty rings to the RT 3 D loops of the mitral valve to select the size of the annuloplasty ring.(see fig 1). The size of the annuloplasty ring determined by one echocardiographer using ring-tool before cardiopulmonary bypass was compared with the actual annuloplasty-ring size implanted by the surgeon who was blinded for the RT 3D data. At the end of the operation another RT 3 D TEE was performed and the size of the implanted annuloplasty ring was determined with ring tool®. The echocardiographer was blinded for the implanted ring size.

Results: After approval by the local ethic committee and written informed consent 53 (39 m/ 14 f) patients with a mean age of 58.2 ± 13.8 years were included in the study. Image quality of the RT 3D TEE was excellent in 57%, good in 17% and poor in 6 % of the patients. All patients received a Carpentier Edwards Physio® annuloplasty ring. In 37 patients the implanted ring size and the selected ring size with ring-tool showed no difference; in 8 patients the ring size selected with ring-tool was 2 mm larger than the implanted ring size and in 8 pts the implanted ring size was 2 mm smaller. The correlation between the selected annuloplasty ring size with the software ring-tool and the actual implanted ring size was 0.91 preoperatively and 0.96 postoperatively.

Conclusion: Real Time 3D TEE correlates well with the standard of surgical sizing. In comparison with 3D reconstruction RT 3D TOE is less time consuming and image quality is improved. The correlation with actually implanted ring size is higher for RT 3D as compared to 3 D reconstruction¹; preoperatively (0.91 vs 0.83) as well as postoperatively (0.96 vs 0.94). To evaluate the clinical value of real time 3 D TOE prospective studies are necessary.

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RED CELL MASS IS NOT WELL CONSERVED FOLLOWING ELECTIVE CARDIAC SURGERY DESPITE USE OF CELL SALVAGE AND TRANSFUSION GUIDED BY PERIPHERAL HEMATOCRIT

Nelson M; Spiess B; Kearney J; Reddy P; Green J; Brinster D; Nicolato P; Kasirajan V

Virginia Commonwealth University

Purpose

Peripheral blood hematocrit (pHct) is commonly used as a measure of red cell volume and to guide transfusion decisions during cardiac surgery. The decrease in pHct accompanying surgery could be due to excessive administration of non-RBC volume expanders or surgical blood loss. We hypothesized that red blood cell volume (RBCV) would be well conserved during surgery – despite marked decreases in pHct – due to cell salvage and transfusion practices. We examined the extent of RBCV loss during surgery and assessed the correlation of pHct with actual RBCV.

Methods

A series of three direct blood volume measurements were performed on 36 patients: (1) before surgery; (2) immediately after surgery; and (3) 2 hours after transfer to the ICU. Total Blood Volume (TBV), Red Blood Cell Volume (RBVC) and Plasma Volume (PV) were measured using the indicator dilution technique via a commercially available, FDA approved semi-automated system (BVA-100 Blood Volume Analyzer, Daxor Corporation).

Results

Despite the use of surgical blood salvage and pRBC transfusions, patients had an average net loss of 675 ± 414 mLs ($p < 0.0001$) of RBCV following cardiac surgery. Male patients showed an average net loss of 813 ± 402 mLs ($p < 0.0001$) while females showed an average net loss of 399 ± 291 mLs ($p = 0.0035$) RBCV. The average net loss of RBCV in 16 patients undergoing coronary artery bypass was 588 ± 447 mLs ($p < 0.0001$). Regression analysis showed only a mild correlation of pHct with RBCV post-surgery ($R^2 = 0.3625$). Normalization of the Hct (which adjusts for abnormally low or high blood volume due to plasma volume derangements) strengthened this correlation ($R^2 = 0.646$)

Conclusions

Direct blood volume measurement can be used to identify deficits/excesses in RBCV that are not evident from the pHct. Our findings showed a strikingly higher loss of RBCV than was hypothesized, particularly in male patients. In patients with blood volume abnormalities – which most of these surgical patients exhibited – the pHct does not provide an accurate estimate of RBCV.

RELATIONSHIP OF IMPAIRED COGNITION BEFORE CARDIAC SURGERY WITH CEREBRAL ISCHEMIA

Maekawa K; Goto T; Fujimoto M; Nonaka T; Otomo S; Baba T

Ito Dento-Maxillofacial Hospital; Kumamoto Chuo Hospital

Background: Cognitive dysfunction is frequent after cardiac surgery, yet preoperative cognitive states have not been studied closely. Postoperative cognitive dysfunction may be associated with preoperative cognitive state and existing cerebral ischemia in patients who undergo coronary surgery.

Methods: 362 patients were enrolled prospectively and consecutively in the present study. All patients were scheduled to undergo coronary artery bypass grafting with (on-pump) or without (off-pump) cardiopulmonary bypass, mitral valve repair or replacement, or aortic valve replacement. All patients had conventional magnetic resonance imaging before surgery to assess prior cerebral infarctions and white matter lesions of the brain. Diffusion-weighted imaging (DWI) was used to assess acute cerebral ischemia. Cognitive state was measured using four tests before surgery and on the seventh postoperative day. Preoperative cognitive impairment was defined as a Hasegawa-dementia score (HDS) less than 24. We compared the incidence of postoperative cognitive dysfunction and systemic atherosclerosis between two groups of with and without preoperative cognitive impairment.

Results and Discussion: Preoperative cognitive impairment by HDS was present in 40 of the 362 patients (11%). Patients who had impaired cognition before surgery were older, had attained less education, and had significantly higher rates of peripheral vascular disease (25% vs. 7%), cerebral infarction on MRI (50% vs. 27%), white matter lesions (65% vs. 46%), carotid artery stenosis (22% vs. 8%), and postoperative cognitive dysfunction (38% vs. 19%) than all other patients. Of the patients with cognitive impairment 7 (18%) had cerebral ischemic lesions on DWI before surgery, and 1 had a perioperative stroke and developed new focal neurological symptoms and signs. An analysis by stepwise logistic regression demonstrated that the significant risks for cognitive impairment were advanced age, lower attained level of education, peripheral artery disease, prior cerebral infarctions and DWI abnormalities. Psychometric tests, such as HDS, may be useful to identify asymptomatic cerebral infarctions in patients undergoing cardiac surgery.

Conclusions: The findings suggest that preoperative cognitive impairment is associated with preexisting cerebral ischemia and an increased risk of postoperative cognitive dysfunction in patients who undergo cardiac surgery.

RESISTANCE TO ISCHEMIC PRECONDITIONING IN RAT ISOLATED HEARTS IS GENETICALLY DETERMINED

Nabbi R; Kersten J; Stowe D; Lazar J; Boelens A; Riess M

Medical College of Wisconsin

INTRODUCTION: Ischemic Preconditioning (IPC) increases resistance to the deleterious effects of subsequent myocardial ischemia and reperfusion (IR) injury (1). However, genetic background may be a confounding factor in the outcome of cardioprotective strategies like IPC. Using an established rat model of genetically determined resistance to IR injury (2,3) we tested the hypothesis of a genome-dependent resistance to IPC.

METHODS: Langendorff-prepared hearts from eight week old male Brown Norway (BN) and Dahl Salt Sensitive (SS) rats (2,3) were used to measure ventricular and coronary function before, during and after 25 min of global no-flow ischemia followed by 120 min reperfusion. IPC was achieved by two 5-min periods of ischemia with 5 min reperfusion interspersed and ending 15 min before prolonged ischemia. Control hearts were not preconditioned. Infarct size was determined by TTC staining and cumulative planimetry. Preliminary data (see table) from 16 animals are expressed as mean[SPCHAR(plusmn)]SEM of % baseline at 120 min reperfusion. Statistics: ANOVA with Student-Newman-Keuls; $P < 0.05$; [SPCHAR(lowast)] vs Con, [SPCHAR(dagger)] vs BN.

RESULTS: IPC resulted in a significant improvement in left ventricular developed pressure and contractility, and decreased infarct size in BN hearts but not in SS hearts after 120 min reperfusion whereas coronary flow was not affected by IPC. Overall, BN control hearts tended to perform better than SS control hearts.

CONCLUSION: Our study shows for the first time that BN hearts, in addition to the previously reported increased resistance to IR injury (2,3), can indeed be protected by IPC whereas SS rats are resistant to cardioprotection by IPC. These results suggest a strong genetic dependence for endogenous cardioprotective signaling and provide a model for a more in-depth investigation of the genetic mechanisms of preconditioning using consomic and congenic animal models.

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RESISTIN AND RESISTIN-LIKE MOLECULE BETA (RELM-B): NOVEL PLEIOTROPIC CYTOKINES IN CARDIAC PATHOPHYSIOLOGY, A REVIEW AND INITIAL FINDINGS

Benneh N; Johns R; Angelini D; Champion H

Johns Hopkins Hospital; Johns Hopkins University, School of Medicine; University of Pittsburgh School of Medicine

INTRODUCTION AND BACKGROUND: Resistin is a recently discovered adipocytokine implicated in inflammation and insulin resistance. A family of resistin like molecules (RELMs) exists in humans and rodents (Teng et al, Steppan et al, Angelini et al). In rodents, we have found RELM β to be upregulated in pulmonary vasculature and right heart in models of pulmonary hypertension (PH)(Teng et al, Angelini et al). Intratracheal administration of RELM β induces all aspects of PH including vessel remodeling, cardiac hypertrophy and impaired diastolic function. RELM α , the human analog of RELM β is upregulated in the lung of human PH. We now look at the expression of RELM α in myocardial biopsies from patients with cardiac hypertrophy or cardiac failure and review the literature on RELMs in human heart disease.

METHODS: We reviewed the limited literature on RELM's in normal and diseased heart conditions. Experimentally, we obtained human ventricular samples by surgical biopsy from patients with cardiac hypertrophy and no evidence of systolic dysfunction and from explanted hearts at the time of transplantation/ left ventricular assist device (LVAD) implantation in patients with severe dilated cardiomyopathy. Normal heart samples were obtained from donor hearts that did not go on to transplantation. All uses of human tissue were approved by the Johns Hopkins IRB.

RELM α mRNA was determined by quantitative reverse transcriptase polymerase chain reaction and protein measured by western analysis and immunochemistry. **RESULTS:** RELM α mRNA and protein were upregulated in patients with cardiac hypertrophy and heart failure (Fig a). In one patient whose failing left ventricle was unloaded with LVAD placement, elevated expression of RELM α was markedly reduced (Fig b). In addition, literature review showed that higher levels of resistin may play a role in future cardiovascular death in patients with acute coronary syndromes (ACS).

CONCLUSIONS: 1. Resistin and its related family members are recently discovered cytokine-like molecules in cardiovascular pathology and atherosclerosis. They have been identified as a possible diagnostic marker for ACS and may correlate with future cardiovascular death. 2. RELM α is upregulated in myocardium of patients with cardiac hypertrophy and heart failure. In one patient with dilated cardiomyopathy it was reduced following unloading of the ventricle with an LVAD. Given the pro-mitogenic action of RELM's in vascular smooth muscle, RELM α may play a mechanistic role in cardiac hypertrophy and failure.

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FIGURE LEGEND: a) Expression of RELM α protein and mRNA in cardiac hypertrophy and heart failure. b) Human expression of RELM α (green fluorescence) in loaded and unloaded failing ventricle.

RESTRICTIVE DIASTOLIC DYSFUNCTION IS PREDICTIVE OF DIFFICULT SEPARATION FROM CARDIOPULMONARY BYPASS: A CASE CONTROL ANALYSIS

Couture P; Toledano K; Denault A; Fernandes A; Levesque S; Babin D; Lebon J; Deschamps A; Qizilbash B; Ayoub C; Cogan J; Rochon A; Bélisle S; Denault A

Montreal Heart Institute

INTRODUCTION: Restrictive filling patterns after cardiac surgery have been shown to be an independent predictor of adverse cardiac events and outcome(1). Furthermore, diastolic dysfunction (DD) has been correlated with difficult weaning from cardiopulmonary bypass (CPB) (2). It is unclear if more advanced DD is associated with more difficult separation from cardiopulmonary bypass (DSB). The objective of this study was to assess whether a restrictive pattern of DD predicts DSB and short-term outcome after CPB.

METHODS: A case-control study was conducting matching patients with restrictive DD undergoing cardiac surgery with patients without restrictive DD. The patients were matched for age, sex, procedure, and duration of CPB. All patients having undergone CPB with restrictive DD on intraoperative echocardiogram between 2000-2007 were identified (n = 42). Of these, the patients with cardiac tamponade, pacing abnormalities, as well as patients undergoing cardiac transplants were excluded. Nineteen patients with restrictive DD were analysed and matched with 19 controls. The primary outcome was DSB as previously defined by Denault et al. (2, 3, 4). The secondary outcomes were duration of vasopressor or inotrope use, intensive care unit (ICU) length of stay, and hospital length of stay. The demographic, echocardiographic, and hemodynamic variables were analysed with the use of logistic regression analysis to determine the independent predictors for difficult separation from CPB and the need for postoperative vasoactive support.

RESULTS: 79% (n=15) of patients with restrictive DD were classified as DSB while 37% of patients without restrictive DD experienced DSB (p = 0.0377). Patients with difficult separation from CPB were 5 times more likely (odds ratio = 5, 95% confidence limit 1.095-22.82) of having restrictive DD than patients without DSB. For every increase in degree of separation from CPB, patients were 2.2 times more likely to have restrictive DD (p=0.0223). There was a trend towards patients with restrictive DD requiring more vasoactive support at 24 hours (53% versus 21%, p = 0.0687).

CONCLUSION: A restrictive pattern of diastolic dysfunction is correlated with difficult separation from CPB. Patients with DSB were 5 times more likely of having restrictive DD than patients without DSB. Future studies to assess whether specific treatments of the restrictive dysfunction can prevent the adverse morbidity associated are necessary.

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RETROSPECTIVE STUDY OF THE INCIDENCE OF SEIZURES IN PATIENTS RECEIVING TRANEXAMIC ACID FOR CARDIAC SURGERY.

Mitchel L; Abel E; Blais D; Torma B; Andritsos M

The Ohio State University Medical Center

BACKGROUND: Over the past 2 years tranexamic acid (TA) use has increased. Since TA has the potential to increase risk of seizure activity, patients with impaired renal function may be at increased risk of seizures because it is primarily excreted renally unchanged (>95%). The purpose of this retrospective study was to determine the incidence of seizures in patients undergoing CPB who received TA. **METHODS:** Using the STS database, all patients undergoing CPB from November 1, 2007 to July 31, 2009 at our institution were included. Our pharmacy database was used to determine those patients who received TA. A 100 mg/kg bolus of TA (maximum dose of 10 gm) was given after heparin administration and prior to CPB. The TA dose was renally adjusted based on creatinine clearance (CrCl) using preoperative serum creatinine. Patients with a CrCl of 20-40 ml/min received a 20% dose reduction and those with a CrCl below 20 ml/min or a history of chronic hemodialysis received a 40% dose reduction. A post-operative seizure was defined as that requiring initiation of anticonvulsant therapy within 48 hours of surgery. The pharmacy database was used to determine which patients received anticonvulsants (phenytoin, fosphenytoin, valproic acid, levetiracetam) in the perioperative period. Benzodiazepine use was not evaluated as anticonvulsant therapy. Patient charts were reviewed to differentiate patients with pre-existing seizure history and those with new onset seizures postoperatively. Confounding variables such as type of surgery, degree of renal dysfunction, pre-existing seizure history, and meperidine use were also collected to determine influence upon risk of seizure. Association between seizure and confounding variables was determined using a two sample t-test or Chi-square test /Fisher exact test as deemed appropriate. A logistic regression analysis will be used to further establish association. **RESULTS:** During the study period, 1060 patients underwent surgery requiring cardiopulmonary bypass, with 756 receiving tranexamic acid. Association of administration of TA and incidence of seizures was statistically significant ($p=0.01$). Of the 756 patients receiving TA, 31 (4.1%) had clinical evidence of seizures while only 3 (1%) of the 304 patients not receiving TA had seizures. Preliminary analyses investigating the association of TA and seizures with subgroups of CABG, any aortic procedure, any aortic or mitral procedure, and VAD did not show a statistical difference. The use of meperidine ($p=0.003$) and previous history of seizures ($p=0.005$) were associated with incidence of postoperative seizure. A logistic regression analysis will determine the association of type of surgery, degree of renal dysfunction, perioperative meperidine, and age on the incidence of seizures in patients receiving and not receiving TA. **CONCLUSION:** Patients receiving TA had a statistically significant higher incidence of seizures. This rate of 4.1% is similar to the 4.6% seen in previous studies. Completion of our regression analysis will serve to better identify factors that increase the risk of seizures in patients receiving TA and tailor pharmacotherapy accordingly. These results will better direct prospective studies analyzing TA in varying doses.

SERUM LACTATE LEVEL DON NOT PREDICT MORTALITY APPROPRIATELY AFTER ADULT CARDIAC SURGERY

Rojas E; Zavala J; Vargas C; Cifuentes C; Barrera M; Suarez L; Figueroa J; Molina F; Lespron M; Hernández M

Institute National of Cardiology

SERUM LACTATE LEVELS DO NOT PREDICT MORTALITY APPROPRIATELY AFTER ADULT CARDIAC SURGERY

Ma. del Carmen Lespron, Marisol Hernández, Francisco J Molina, Javier Figueroa, Lorena Suárez, Marcela Barrera, Carlos Cifuentes , Carlos Vargas, José A Zavala, Eduardo M Rojas
Instituto Nacional de Cardiología "Ignacio Chávez". México City. México

Objective. To describe serum lactate levels in adult patients undergoing cardiac surgery with cardiopulmonary bypass and assess if they can appropriately predict mortality.

Methods. From 2005 to 2008, 636 adult patients subjected to elective primary coronary revascularization or valvular surgery were studied. Inclusion criteria were: age from 18 to 75 years, ejection fraction greater than 40%, absence of infection and organ dysfunction. Blood samples for serum lactate measurement were obtained at baseline (before surgery), post-bypass, at intensive care unit (ICU) admission and at 6, 12, 24 and 48 hours after ICU admission. The primary outcome was in-hospital mortality. Serum lactate variations over time and between groups (alive vs dead patients) were analyzed by MANOVA. ROC curves were used to define lactate's ability to predict mortality.

Results. Mortality in this group was 4.38% (28 patients). Lactate values presented a significant change over time ($p=0.000$), with the highest mean concentrations and difference between groups at 6 hours of ICU admission (alive 4.08 ± 2.1 vs dead 5.08 ± 2.3 mmol/l; $p 0.014$). These lactate values were able to discriminate alive and dead groups with an area under the curve of 0.63 (95%CI 0.51-0.74; $p 0.020$). Derived from the ROC curve, a lactate value of 4.5 mmol/l had a sensitivity of 35.7% and a specificity of 64.1%

Conclusions. Mean serum lactate levels after adult cardiac surgery had their highest values at 6 hours of ICU admission and were significantly higher in patients who died. However, lactate does not predict appropriately mortality. A greater number of patients are needed to confirm these results.

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Figure 1. Serum lactate's behavior in 636 cardiac surgery patients

SEX, AUTONOMIC DYSFUNCTION, COMPLEX CARDIAC SURGERY AND THE RISK OF PERIOPERATIVE DECREASES IN CEREBRAL OXYGEN SATURATION

Deschamps A; Rochon A; Lebon J; Ayoub C; Qizilbash B; Couture P; Cogan J; Toledano K; Pagé P; D'Antono B; Denault A

Montreal Heart Institute, University of Montreal

Introduction: Near-infrared reflectance spectroscopy (NIRS) is used as a non-invasive and continuous monitor of cerebral oxygen saturation (rSO₂). The use of NIRS can lead to shorter recovery room and hospital stay in non-cardiac surgery (1), and in a decrease in major organ dysfunction and in the length of stay in the intensive care unit after coronary bypass surgery (2). Significant decreases in perioperative rSO₂ values are associated with post operative neurocognitive dysfunction (3). Although the importance of monitoring rSO₂ is becoming recognized, little is known about the predisposing factors for perioperative decreases in rSO₂. Furthermore, most studies have focused on primary CABG surgery and the incidence of decreases in rSO₂ in cardiac surgery in general is not described. We hypothesized that autonomic dysfunction would predispose patients to decreases in rSO₂ and that the prevalence of cerebral desaturation would be greater in cardiac surgery in general than in primary CABG surgery only.

Methods: Informed consent was obtained for this study. Prospective NIRS values were collected on 90 patients scheduled for cardiac surgery with cardiopulmonary bypass (CPB). Autonomic dysfunction was assessed in 70 of these patients by an abnormal response to the Valsalva maneuver (VAL) and baseline heart rate variability (HRV) (4). The anesthesia strategy was standardized. The anesthesiologist was blinded to the NIRS values and therefore no intervention was made to reverse decreases in rSO₂. A significant decrease in rSO₂ was defined as a fall >20% from baseline values for 1min or longer.

Results: Ninety patients, 75 men and 15 women (42-82 years old) participated in the study. Baseline NIRS values ranged from 48 to 87%. Significant decreases in rSO₂ occurred in 52 (57.8%) patients, 38 (51%) men and 14 (93%) women (RR=10.231, CI:1.41-74.52). Decreases in rSO₂ were more common in complex surgeries (redo, valves or valves and CABG, 41/52, RR=1.665, CI:1.157-2.394) than with primary CABG (11/31). There was no relationship between decreases in rSO₂ and age, duration of CPB or Parsonnet score. Of the 70 patients tested for autonomic dysfunction, 38 (54.3%) had a normal VAL response and 32 (45.7%) had an abnormal VAL response. Decreases in rSO₂ occurred in 75% (24:32, 6 women) of patients with an abnormal VAL response compare to 47.4% (18:38, 6 women) in those with a normal VAL response (RR=2.0, CI:1.053-3.799).

Discussion: The incidence of decreases in rSO₂ appears to be higher when complex surgeries are included 58% vs 30%(3). Women have a significantly higher risk of intraoperative decrease in rSO₂. Patients with autonomic dysfunction prior to surgery also have a higher risk of decreases in rSO₂ intraoperatively. The reasons why women have a higher risk of decrease in rSO₂ remains to be elucidated and whether interventions to correct autonomic dysfunction before surgery would decrease the incidence of cerebral desaturations deserves to be tested.

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SIZE AND FUNCTION OF LEFT AND RIGHT VENTRICLES IN SEPTIC ICU PATIENTS: A CLINICAL ECHOCARDIOGRAPHIC BIOCHEMICAL STUDY

Landesberg G; Landesberg G; Giorgieva M; Meroz Y

Hebrew UNiversity - Hadassah Medical Center

Background: Sepsis is a common disease with a prevalence of 240 cases per 100,000 people in the USA. The death rate from sepsis in the USA is equal to and even greater than the death rate from acute MI. However, while the mortality from myocardial infarction is constantly decreasing, mortality from sepsis remained almost constant in the last decades, despite the advancements in medical treatment.

Cardiovascular dysfunction plays a major role in the morbidity and mortality from severe sepsis and septic shock. Yet, the exact mechanisms causing cardiac dysfunction in sepsis are still in major part obscure or controversial. The purpose of the present study was to provide a detailed characterization of left ventricular systolic and diastolic functions, their clinical and biochemical correlates and their effect on patient survival.

Methods: In this observational study, data was collected prospectively from consecutive septic patient above the age of 18, who were admitted our intensive care units. All patients who had the criteria for severe sepsis or septic shock underwent daily transthoracic echocardiography examinations from which detailed data on left ventricular end-diastolic, end-systolic volumes areas, diastolic measurements were obtained. In addition, numerous clinical, hemodynamic, respiratory and laboratory data were prospectively collected, including data on survival up to 2 years after admission. Blood samples were collected, centrifuged and serum separated for additional biomarker tests, mainly troponin and NT-proBNP. Statistical analyses included Cox's proportional hazards (univariate and multivariate) survival analyses and Kaplan-Meier, Log-rank tests.

Results: All together 262 patients underwent 712 (2.5±1.4) transthoracic echocardiography examinations. Mean APACHE score was 20.6±7.3 and 41% had positive blood cultures. More than 40% of the patients died within the first 4 months of admission to the ICU.

Numerous echocardiographic systolic and diastolic, left ventricular measurements predicted mortality by univariate Cox's survival analysis.

On multivariate analysis, age, APACHE score, heart rate, isovolumic relaxation time, NT-proBNP and positive blood cultures were associated with increased mortality whereas end diastolic volume, stroke volume, LV ejection fraction and all tissue-Doppler parameters of mitral annular velocities were associated with improved survival. On multivariate Cox's survival analysis LC ejection fraction, end-diastolic volume and Em wave on tissue Doppler imaging independently predicted improved survival and heart rate independently predicted worse survival (Exp(B) = 0.009, 0.969, 0.9, 1.004 and p value = <0.0001, <0.0001, 0.001, 0.002, respectively). Only 45% of patients with end-diastolic volume index < 40 ml survived more than 4 months, compared with 75% survival in patients with end-diastolic volume index > 54 ml.

Conclusions: Echocardiographic measurements strongly predict early survival in patients with severe sepsis and septic shock. Particularly decreased ejection fraction, decreased end-diastolic volume, diastolic dysfunction and tachycardia independently predict mortality. Further studies will show if treating those parameters can improve survival.

STORAGE AGE OF TRANSFUSED RBCS ON ACUTE KIDNEY INJURY IN CARDIAC SURGERY

Hathaway J; Stafford-Smith M; Phillips-Bute B; Gaca J; Swaminathan M; Shaw A; Hill S; Welsby I

Duke University Medical Center

Introduction – In cardiac surgery, acute kidney injury (AKI) is a significant predictor of mortality [1] and both AKI and mortality are associated with RBC transfusion [2],[3]. These effects are increased when the age of the transfused blood is greater than two weeks [4]. However, it is unclear if the relationship between age of blood and AKI holds true when patients are transfused increasing numbers of units of RBCs. Therefore, our hypothesis tested whether the effect of worsening AKI with increasing age of blood persists when adjusting for the number of units transfused.

Methods and Results – With IRB approval, we reviewed data from 4643 primary, non-emergent coronary artery bypass graft (CABG) patients that received ≥ 1 blood transfusion from 1993-2002. Age of the oldest unit transfused was used as a marker for the recipient burden of aged blood. The association between the age of the oldest unit and AKI was assessed with multivariable linear regression with % delta creatinine, calculated as $((\text{max postop cr} - \text{preop cr})/\text{preop cr}) * 100$. We found a univariate association between the storage age of the oldest unit transfused and the degree of AKI ($p=0.0005$); however, this effect becomes marginal after adjusting for the total number of units transfused ($p=0.0515$). Total units transfused is a highly significant predictor of the % delta creatinine ($p<0.0001$). The figure, based on predicted values from the multivariable regression analysis, shows the association of age of oldest unit of blood and % delta creatinine for four different levels of transfusion. Restricted cubic splines are included in the model to allow for non-linearity of the association. The figure suggests that % delta creatinine increases when the age of blood is older than approximately 14 days.

Discussion – The association of older blood with AKI is marginalized by adjusting for the number of units transfused. As the figure suggests, there is a positive relationship between both variables and AKI, but only number of units has an independent association with AKI. The apparent association of age of blood and AKI may be explained by the increased likelihood of receiving older unit(s) of blood with increasing numbers of transfused units. The figure also illustrates the suggested relationship between storage age and AKI that appears to develop after about 14 days, consistent with prior observations [4]. Further defining of this relationship will be pursued in a larger dataset and prospective study is needed to determine causation rather than association between transfusion and organ injury.

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THE DEGREE OF MYOCARDIAL INJURY DURING OPCAB SURGERY: SEVOFLURANE VERSUS PROPOFOL-SUPPLEMENTED REMIFENTANIL- BASED ANESTHESIA

Song J; Kim T; Yoon T; Kim S; Chi H; Shin J

Konkuk University Medical Center

Background: Remifentanil-based anesthesia for the off-pump coronary artery bypass (OPCAB) surgery requires supplementation of other anesthetics to ensure sufficient intraoperative amnesia. The present study was designed to determine the degree of myocardial injury following the supplemental use of sevoflurane versus propofol for the remifentanil-based anesthesia during OPCAB surgery.

Methods: Patients undergoing the elective OPCAB surgery were randomly allocated to get one of two anesthetic regimens: sevoflurane-supplemented remifentanil-based (Group SR, n = 47) or propofol-supplemented remifentanil-based regimen (Group PR, n = 47). In both groups, etomidate 1-1.5 µg was administered and followed by remifentanil infusion (1.0 µg/kg/min). The dosage of supplemental sevoflurane or propofol was adjusted to maintain bispectral index (BIS) at 40-60. As an indicator for myocardial injury, creatine kinase MB (CK-MB) and troponin I (TnI) were measured before (T0) and after surgery: at the admission to the ICU (T1) and 12 and 24 hours after the ICU admission (T2 and T3).

Results: There were no significant inter-group differences in patient demographic data including age, sex, number of grafts, anesthesia time, operation time, extubation time and ICU stay. CK-MB and TnI at T1, T2 and T3 were significantly higher than those of T0 in both groups, but there were no significant intergroup-differences of those at each time period. (Table)

Conclusion: Supplementation of sevoflurane or propofol to the remifentanil-based regimen for achieving sufficient intraoperative amnesia did not show any difference in terms of reducing myocardial injury during OPCAB surgery.

THE EFFECT OF 6% HYDROXYETHYL STARCH 130/0.4 ON BLOOD LOSS AND COAGULATION IN PATIENTS TREATED WITH CLOPIDOGREL PRIOR TO OFF-PUMP CORONARY BYPASS GRAFT SURGERY

Ahn S; Kim J; Yoo Y; Shim J; Kwak Y

Yonsei University College of Medicine

Background: Clopidogrel and aspirin reduce thrombotic complications in patients with coronary artery obstructive disease and favorable results regarding prevention of recurrent ischemic events leading to reduced risk of cardiovascular morbidity and mortality have been demonstrated. As the indications for clopidogrel expand, an increasing percentage of patients presenting for coronary artery bypass graft surgery (CABG) are subjected to irreversible platelet inhibition and thus, have a higher risk of bleeding complications and transfusion requirements. The currently developed hydroxyethylstarch (HES) solution with low molecular weight and molar substitutions, HES 130/0.4 was demonstrated to have less effect on coagulation than its congeners. The purpose of this study was to evaluate whether HES 130/0.4 significantly affect coagulation and blood loss in patients medicated with clopidogrel prior to off-pump coronary bypass surgery (OPCAB).

Methods: Eighty patients undergoing OPCAB, who were exposed to clopidogrel with or without aspirin until 5 days prior to surgery were randomly allocated to infuse HES 130/0.4 up to 30 ml/kg and followed crystalloid infusion (HES group, n = 40) or infuse crystalloid only (Crystalloid group, n = 40) during perioperative period. Fluid replacement was guided by cardiac index (> 2.2 l/min/m²) and pulmonary artery wedge pressure (10-14 mmHg). Preoperative thromboelastography (TEG) and other coagulation variables were measured and follow up data were collected at immediate postoperatively and 24 hours after surgery. Perioperative blood loss, amount of transfusion and fluid balance were recorded.

Results: The two groups were similar in demographic and operative data. There were no significant differences in coagulation variables including TEG results, blood loss and transfusion between the groups during operation and postoperative 24 hrs (Table 1).

Conclusion: HES 130/0.4 solution in patients undergoing OPCAB who were exposed of clopidogrel until 5 days prior to surgery did not adversely affect coagulation and not significantly increase blood loss and transfusion requirement compared to crystalloids.

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THE EFFECT OF CLODRONATE AND DIFFERENT LEVELS OF HYPOTHERMIA DURING CARDIAC ARREST ON TNF α LEVELS IN SELECTED BRAIN REGIONS IN RATS

Drabek T; Janata A; Stezoski J; Jackson E; Janesko-Feldman K; Wilson C; Tisherman S; Kochanek P

University of Pittsburgh

Background: Prolonged cardiac arrest (CA) produces neuronal death that is associated with microglial proliferation and activation. Microglia are a major source of pro-apoptotic cytokine TNF α . Thus, early inhibition of microglia could be beneficial. We previously showed that microglia proliferation is attenuated by deep hypothermia or intrahippocampal injection of liposome-encapsulated clodronate.(1,2) In this study, we hypothesized that 1) brain tissue TNF α would be decreased with deeper hypothermia; 2) direct injection of clodronate into the hippocampus would decrease TNF α level in hippocampus after CA in rats.

Methods: Isoflurane-anesthetized male adult rats (n=6 per group) were stereotactically administered 10 μ L of liposome-encapsulated clodronate or liposome-encapsulated PBS into the right or left hippocampus, respectively. 24 h later, rats were subjected to rapid exsanguination followed by 6 min of CA. Hypothermia was then achieved with a flush of either ice-cold (IC) or room-temperature (RT) Plasma-Lyte A (270 ml) into the aorta. After a total of 20 min CA, resuscitation was achieved via cardiopulmonary bypass. Rats were sacrificed at 24 h. Brain TNF α levels were analyzed by ELISA in cortex, striatum, hippocampus and cerebellum separately in each hemisphere.

Results: During CA, the temperature decreased to 21.3 \pm 2.6 $^{\circ}$ C after IC flush vs. 28.9 \pm 3.1 $^{\circ}$ C after RT flush, respectively. There were significant regional differences in TNF α levels between individual brain regions in both groups, with the highest levels seen in striatum and cerebellum (Figure). TNF α levels were significantly decreased in the IC group vs. RT group in right cortex and right striatum, respectively (* p < 0.05). There were no differences between right vs. left hippocampus.

Discussion: Our data suggest a robust effect of deep hypothermia on brain TNF α levels after CA, corroborating the effects on microglia. Our previously documented clodronate-induced attenuation of microglial proliferation did not result in decreased TNF α levels in hippocampus. The levels of TNF α were overall very low, compared to levels observed after stimulation of microglia with endotoxin.(3) Surprisingly, the increase of TNF α was seen in striatum, cerebellum and cortex but not hippocampus despite marked neuronal death in CA1 in this model. Exploring the effects of clodronate in striatum might be the best target for future studies of the role of microglia in hypothermic CA.

Supported by the Society of Cardiovascular Anesthesiologists (TD), American Heart Association 09BGIA2310196 (TD), NS 38087 and NS 30318 (PMK).

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THE EFFECT OF SINGLE-DOSE ETOMIDATE FOR ANESTHETIC INDUCTION ON ADRENAL FUNCTION AND CYTOKINE RESPONSE IN OFF-PUMP CORONARY ARTERY BYPASS SURGERY

Barron M; Nhuch F; Vaughn J; Rodriguez Y; Candiotti K

UM/ JMH

Etomidate blocks adrenal steroidogenesis and infusions have been implicated as a causative agent of adrenal insufficiency and increased morbidity and mortality. Also of concern, is the finding by Zurick et al. that a single dose of etomidate produced adrenal suppression in adults undergoing surgery with cardiopulmonary bypass (CPB). Etomidate may not only induce adrenal insufficiency, but also amplify the inflammatory state and contribute to poor outcomes.

Following CPB there is a proinflammatory state marked by the release of cytokines and inflammatory mediators into the circulation. For instance, IL-6 affects coagulation, increasing tissue factor and factor VIII levels, enhancing platelet production, and increasing the transcription of the fibrinogen gene. Additionally, IL-6 promotes inflammation and increased IL-6 levels after CPB are predictive of infection after cardiac surgery.

The influence of a single induction-dose etomidate on adrenocortical and inflammatory cytokine responses following off-pump coronary artery bypass (OPCAB) has not been established and was the purpose of our study.

Methods:

After IRB approval and signed informed consent, patients 18 to 80 years of age scheduled to undergo elective OPCAB, were randomized to receive either etomidate or propofol for induction of general anesthesia. A total of 17 patients were enrolled, 10 in the etomidate arm and 7 in the propofol. Blood was collected for measurement of serum cortisol and cytokines at baseline (pre-induction), 30 minutes, 2 hours, 8 hours after sternotomy and 24 hours after last stitch.

All blood samples were obtained via arterial line and were collected in 10 mL evacuated tubes containing EDTA. Samples were immediately placed on ice, centrifuged at 4°C within one hour of collection, and the serum was stored at -80°C. Serum concentrations of cortisol, IL-6 were measured using commercially available ELISA kits.

Results:

Baseline levels of cortisol and IL-6 were similar for both groups. At 8 hours patients in the etomidate group were noted to have significantly lower levels of cortisol as well as significantly increased levels of IL-6 with respect to baseline when compared to patients receiving propofol. No statistically significant differences were detected between the two groups at 24 hours. (Chart 1)

Discussion:

Our findings suggest a transient adrenocortical suppression and a significant increase in IL-6 levels in the first 24 hrs after a single induction dose of etomidate, compared to propofol, in patients undergoing OPCAB. Our findings are consistent with other studies utilizing etomidate in critically ill patients and patients undergoing on pump cardiac surgery. A larger sample size and outcomes evaluation would appear indicated based on our preliminary data.

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THE EFFECT OF TRANEXAMIC ACID ON BLOOD LOSS IN PATIENTS WITH PREOPERATIVE ANEMIA UNDERGOING OFF-PUMP CORONARY ARTERY BYPASS GRAFT

Ahn S; Kim J; Yoo Y; Shim J; Kwak Y

Yonsei University College of Medicine

Background: Preoperative low hematocrit level is the strongest predictor of packed red blood cell transfusion (pRBC), especially in patients undergoing off pump coronary bypass graft (OPCAB). Tranexamic acid (TA), an anti-fibrinolytic drug, is known to reduce postoperative blood loss and transfusion requirements in cardiac surgery with cardiopulmonary bypass. The aim of this study was to evaluate the effect of tranexamic acid on postoperative blood loss, transfusion requirements and coagulation in patients with preoperative anemia undergoing OPCAB.

Methods: Fifty patients undergoing OPCAB with preoperative hematocrit levels lower than 35% were randomized into two groups : the TA group receiving tranexamic acid (1g loading dose before skin incision and continuous infusion 200 mg/h during surgery, n = 25) and the control group receiving the same volume of saline solution (control, n = 25). Salvaged blood from the operating field was administered and pRBC was transfused when hematocrit levels were lower than 25%. Blood loss during 24 hours postoperatively, and the number of patients requiring pRBC transfusion during hospital stay were recorded.

Result: The two groups were similar in demographic and operative data. Intraoperative transfusion, total amount of transfused pRBC and number of patients who received transfusion during hospital stay was significantly lower in the TA group with similar perioperative hematocrit levels, although measurable perioperative blood loss was similar (Table 1).

Conclusion: TA could significantly reduce the amount and incidence of homologous transfusion in anemic patients undergoing OPCAB.

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THE HYBRID CARDIAC SURGICAL ICU: THE IMPACT OF DAYTIME CARDIAC ANESTHESIOLOGIST/24-HOUR IN-HOUSE INTENSIVIST STAFFING ON OUTCOMES AFTER ULTRA-FAST TRACK CARDIAC ANESTHESIA

Kumar K; Gulati H; Heibert B; Zarychanski R; Grocott H; MacKenzie S; Zivot J; Menkis A; Arora R

u; University of Manitoba

Introduction: Fast-track cardiac anesthesia has previously been associated with reductions in intensive care unit (ICU) and total hospital length of stay (LOS). However, the definition of fast-track cardiac anesthesia has been inconsistently used in the literature. At our institution, we routinely plan on extubating patients in the operating room following their cardiac surgical procedure, thus defining ultra-fast track anesthesia. The impact of ICU care on outcomes in these ultra-fast track patients has not been explored. The objective of this study was to determine the impact of a dedicated 24-hour in-house intensivist/cardiac anesthesiologist hybrid ICU model of care on outcome after ultra-fast-track cardiac anesthesia.

Methods: A retrospective cohort analysis of consecutive patients undergoing cardiac surgery at a single tertiary center from Jan 2005 to Jan 2008 was performed. Patients who were extubated in the operating room were identified and separated into two groups: a control cohort (SICU group), that consisted of patients admitted to a traditional mixed surgical intensive care unit (SICU) from Jan 2005 to Jan 2007, and an intervention cohort (CICU group) consisting of patients admitted after Jan 2007 to a newly created hybrid cardiac surgical ICU (CICU) staffed by a dedicated daytime cardiac anesthesiologist and a 24-hour in-house consultant intensivist (Figure 1). Using propensity analysis, the SICU and CICU ultra-fast track patients were compared for a number of perioperative outcomes.

Results: In this study, 2548 consecutive patients underwent cardiac surgery at our institution with 1465 being admitted to the SICU and 1083 to the hybrid CICU. Overall, 1062 (41.7%) of these patients were identified as having been extubated in the operating room at the conclusion of their procedure and were included in this subsequent analysis. 55.8% (604/1083) of CICU patients were extubated in the operating room compared to 31.3% (458/1465) of the SICU patients ($p < 0.001$). Propensity matching of the two ultra-fast-track cohorts demonstrated that compared to the traditional SICU patients, the hybrid CICU model of care was associated with a lower red blood cell (RBC) transfusion rate (17.8% vs. 28.5%, $p < 0.001$), lower fresh frozen plasma (FFP) use (5.0% v 14.9%, $p < 0.001$), and a decrease in overall hospital LOS (5 [4-6] vs. 6 [5-7] days, $p < 0.001$). There was no difference in the need for re-intubation (3.1% SICU vs. 1.6% CICU, $p = .15$) nor need for readmission to ICU (2.6% SICU vs. 1.3% CICU, $p = 0.19$). Furthermore, the CICU cohort demonstrated significantly lower phenylephrine, milrinone, and Pentaspan use following extubation.

Conclusions: The availability of a hybrid cardiac surgical ICU staffed by cardiac anesthesiologists during the day as well as an 24 hour in-house intensivist allowed for a higher operating room extubation rates along with significant reductions in both blood product usage and overall hospital LOS.

THE IMPACT OF PERIOPERATIVE BLOOD PRESSURE CONTROL ON HOSPITALIZATION COSTS IN PATIENTS UNDERGOING CARDIAC SURGERY: RESULTS FROM ECLIPSE

Multz A; Dyke C; Hu M; Wang Y; Williams G; Ferguson J; Getsios D; Ishak J; Alvarez P; Stolar M; Aronson S

Albert Einstein College of Medicine; Brazosport Regional Health System; Duke University Medical Center; The Medicines Company; United BioSource Corporation

Background: Previous studies have shown an association between effective perioperative blood pressure (BP) control and a reduced risk of death and/or adverse clinical outcomes in patients undergoing cardiac surgery. The ECLIPSE (Evaluation of CLevidipine In the Perioperative Treatment of Hypertension Assessing Safety Events) trials compared the newer-generation dihydropyridine calcium blocker clevidipine to nitroglycerin, sodium nitroprusside, and nicardipine in the perioperative management of BP in patients undergoing cardiac surgery. While ECLIPSE showed an association between precise BP control and improved clinical outcomes, it did not prospectively assess the relationship between BP control and hospital costs.

Objective: The ECLIPSE database was used to evaluate the relationship between perioperative BP control and the total costs of hospitalization and 30-day readmission in 1512 patients undergoing coronary artery bypass grafting, valve replacement and/or valve repair surgery, by assigning appropriate hospital costs to individual ECLIPSE patients.

Methods: Cost data were obtained from the Massachusetts Hospital Inpatient Discharge (Case Mix) Database for 2007 for patients undergoing cardiac surgery and analyzed separately for patients who experienced death, myocardial infarction, stroke, bleeding, infections, renal failure, multiple complications, or none of these complications. These data were used to assign 2009 hospitalization costs to the ECLIPSE patients by matching their complications and length of stay. BP control was defined as area under the curve (AUC) capturing the magnitude and duration of systolic BP excursions outside the range of 75-135 mmHg intraoperatively and 85-145 mmHg pre- and postoperatively. AUC was normalized by hour and expressed in units of mmHg×min/h, and ranged from 0 to 1103.8 mmHg×min/h in the study. Smaller AUC values represent more precise BP control with 0 mmHg×min/h indicating BP was always within the range. The association between AUC and costs was examined using a log-normal model, controlling for other potential confounding factors.

Results: Mean estimated costs for patients in ECLIPSE were \$49,567. Patients with an AUC less than 10 mmHg×min/h (N=766, 51.1%) had mean costs of \$46,883 while those with an AUC above 10 mmHg×min/h (N=732, 48.9%) had mean costs of \$52,407. After controlling for potential confounders, a perioperative AUC below 10 mmHg×min/h was associated with 7.2% lower costs (P=0.018). For the population with an AUC greater than 10 mmHg×min/h, reducing AUC to below 10 mmHg×min/h was predicted to reduce costs by \$3,493 (range \$1,820-\$8,184).

Conclusion: Effective perioperative BP control in patients undergoing cardiac surgery is significantly associated with hospitalization costs. Tightly controlling BP may potentially be associated with considerable cost savings in cardiac surgery patients.

THE INFLUENCE OF MEAN BLOOD GLUCOSE MEASUREMENTS ON DIABETIC AND NONDIABETIC PATIENTS UNDERGOING CARDIAC SURGERY

Hargrave J; Duncan A; Xu M

Cleveland Clinic

Introduction: Severe perioperative hyperglycemia is clearly associated with worse outcome. Evidence suggests that hyperglycemia may affect diabetic and nondiabetic patients differently. For example, critically ill diabetic patients did not receive a mortality benefit from intensive insulin therapy in contrast to nondiabetic patients.(1) Further, hyperglycemia had less severe adverse effects on noncardiac surgical patients with diabetes.(2) The purpose of this investigation was to determine whether risk of adverse outcomes related to intraoperative hyperglycemia is similar in diabetic compared to nondiabetic cardiac surgical patients.

Methods: The Cleveland Clinic Cardiothoracic Anesthesia Registry identified 4,302 patients who had cardiac surgery (including coronary bypass grafting and/or valve surgery) between 10/3/2005 and 5/31/2007. Intraoperative time-weighted average glucose levels were calculated for patients with four or more blood glucose measurements. Patients were then placed into the following categories: time-weighted average glucose \leq 140, 141-170, 171-200, or $>$ 200 mg/dL. Patients were further categorized depending on the presence or absence of preoperative diabetes mellitus. The influence of mean glucose on in-hospital mortality and overall morbidity (which included mortality, prolonged intubation, cardiac, renal, infection and neurological complications) was evaluated by multivariable logistic regression with backward selection and adjustment for confounding variables. The model was evaluated for an interaction between the presence of diabetes and the influence of glucose levels on outcomes.

Results: The patient population included 3278 (76.2%) and 1024 (23.8%) nondiabetic and diabetic patients, respectively. Morbidity and mortality in diabetic patients was nearly two to three-fold higher than in nondiabetic patients (Figures 1 and 2). The presence of diabetes increased risk for mortality [odds ratio (95% CI) 1.8 (1.0, 3.2); $P = 0.039$] and morbidity [1.5 (1.1, 2.0); $P = 0.005$]. No interaction was found between diabetic status and the influence of mean blood glucose on outcomes.

Conclusion: Although severe intraoperative hyperglycemia ($>$ 200 mg/dL) was associated with adverse outcome in cardiac surgical patients, decreasing increments of mean glucose did not consistently moderate risk. Diabetes per se was a risk factor for worse outcomes; however, the influence of glucose on outcomes was similar in diabetic and nondiabetic patients.

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THE PERCENT DECREASE IN INTRA-OPERATIVE SYSTOLIC BP FROM BASELINE IS ASSOCIATED WITH THE PERCENT INCREASE IN POSTOPERATIVE CREATININE FOLLOWING CARDIAC SURGERY

Swaminathan M; Shaw A; Phillips-Bute B; Stafford-Smith M; Aronson S

Duke University Medical Center

Background: It has been shown that % change in creatinine is a sensitive index of acute kidney injury and associated with high mortality and substantial additive cost after coronary bypass graft surgery (1, 2). We tested the hypothesis that intraoperative systolic blood pressure variability is associated with postoperative change in serum creatinine.

Methods: 7,247 patients were evaluated in this prospective and descriptive study of patients having coronary bypass graft surgery from Sept. 1996 to Dec. 2005. Measures of systolic blood pressure variability were determined for each patient and were characterized by frequency, magnitude (mmHg), duration (min), area under curve (mmHg*min), and % change from baseline. The study sample was randomly divided into a development cohort (2/3) and a validation cohort (1/3). Each of these was evaluated separately in a linear regression model predicting % delta creatinine, adjusting for covariates (aprotinin use, age, chf, previous mi, baseline creatinine, bypass time, diabetes, weight, valve surgery, gender, and pulse pressure).

Results: The measure most highly associated with % delta creatinine based on model r² value in the developmental sample was % change from baseline SBP to the lowest SBP, p< 0.006 (model r² value =0.005). Multivariable linear regression demonstrated an association between % change in SBP below baseline to % delta creatinine (p< 0.0016) in the validation data set.

Conclusions: The percent change of intraoperative systolic BP below baseline BP is associated with the percent increase change from baseline in creatinine observed following cardiac surgery.

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THE POCKET ECHOCARDIOGRAPH: VALIDATION AND FEASIBILITY

Culp B; Mock J; Chiles C; Culp, Jr. W

The Texas A&M University System Health Science Center College of Medicine/ Scott and White Hospital

Background: Recent studies have shown promising results for point of care echocardiography in the preoperative clinical evaluation with resultant direct changes in management.^[1]^[2] A new, miniaturized ultrasound device, the pocket echocardiograph (PE), is highly portable and can be carried inside a lab coat pocket. Existing studies of this device are limited and have not examined use by novice echocardiographers.^[3] We hypothesize that a less experienced echocardiographer can use PE to produce interpretable cardiac images, and that both novice and expert echocardiographers can use PE to accurately quantify ejection fraction.

Methods: Unselected subjects (n=40) in an echocardiography laboratory underwent blinded formal transthoracic echocardiography (TTE) and PE (Acuson P10, Siemens, USA). A cardiology fellow with two months of echocardiography training, including 120 formal TTE acquisitions and 30 PE exams acquired all PE images. The fellow and an experienced echocardiographer both interpreted PE studies offline in a blinded fashion. To assess adequacy, studies were graded as technically adequate, limited, or inadequate. Visual estimation of ejection fraction was made. Comparisons were made to the formal reported TTE. Ordinal data was analyzed with descriptive and Wilcoxon analysis; continuous data underwent Pearson and Bland-Altman analysis.

Results: Subjects were heterogeneous, 43% male; age 64 ± 17 years, range 18-85, and ejection fraction $52.4\% \pm 12.3\%$, range 15-70%. All PE studies were interpretable, and the vast majority of PE and TTE images were considered technically adequate (77.5% and 85% respectively; $p=0.32$). Ejection fraction showed good correlation, bias, and limits of agreement for the fellow's interpretation ($r=0.78, -5.9\%, \pm 16.6\%$), with even stronger association for the experienced echocardiographer ($r=0.88, -0.8\%, \pm 11.4\%$).

Conclusion: A novice echocardiographer using the PE can produce adequate quality images. Both expert and less experienced echocardiographers can use PE to accurately quantify ejection fraction over a broad range of patients. These limits of agreement are consistent with clinically accepted variances for formal TTE. The device's low cost and portability may greatly expand the availability of bedside echocardiography for routine or urgent cardiovascular assessment, including preoperative evaluation.

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Figure 1. Regression plot showing the correlation between TTE and PE with fellow interpretation.

THE PPAR[SPCHAR(GAMMA)] AGONIST ROSIGLITAZONE AMELIORATES CEREBRAL INFLAMMATION AND APOPTOSIS FOLLOWING EXPERIMENTAL DEEP HYPOTHERMIC CIRCULATORY ARREST

Mackensen G; Ma Q; Zhang Z; Podgoreanu M

Duke University Medical Center

Background: Perioperative cerebral injury (PCI) following major cardiovascular surgery using cardiopulmonary bypass (CPB) and deep hypothermic circulatory arrest (DHCA) remains as significant cause of adverse cerebral outcomes. Potential mechanisms of injury are related to cerebral inflammation and ischemia-reperfusion introduced by CPB and DHCA. Rosiglitazone, an agonist of peroxisome proliferator-activated receptor gamma (PPAR γ), has recently been shown to improve cerebral outcomes from experimental ischemia and reperfusion injury. This study explores a) the involvement of key biological pathways in CPB/DHCA-associated PCI and b) investigates the anti-inflammatory and anti-apoptotic potential of the PPAR γ agonist rosiglitazone in a rat model of CPB/DHCA.

Methods: Male atherosclerosis-prone JCR rats underwent 45 min of DHCA at 18°C and received either vehicle (n=3) or Rosiglitazone treatment of 4mg/kg i.p. 1 hour before CPB and 1 hour after reperfusion (n=4). Brain samples were harvested 24 hours after CPB/DHCA. Microarray profiling (Rat Gene 1.0 ST Array, Affymetrix; 27,342 sequences) was conducted using total RNA from whole brain. Category overrepresentation analysis was used to identify biological pathways deregulated in response to CPB/DHCA. Cerebral levels of PPAR γ protein, phosphorylation of signal transducers and activators of transcription (STAT3) and cerebral levels of cleaved caspase-3 were determined by Western blot. In situ expression of PPAR γ protein was analyzed by confocal microscopy. Using ELISA, DNA binding activity of cerebral PPAR γ ; and nuclear factor kappa B (NF- κ B), cerebral levels of interleukin (IL)-10, IL-1 β , IL-6, and cerebral activity of myeloperoxidase (MPO) were analyzed. TUNEL assay and H&E staining were used to detect apoptotic neurons.

Results: Category overrepresentation analysis identified a deregulated transcriptional network including observed transcriptional changes for PPAR γ ; (figure 1). Pretreatment with Rosiglitazone resulted in consistent anti-inflammatory and anti-apoptotic actions that were accompanied by increased DNA binding activity of PPAR γ ; and inhibited activation of NF- κ B as well as suppressed phosphorylation of STAT3 (table 1).

Conclusions: This study demonstrates a mechanistic role of PPAR γ activation in PCI following CPB/DHCA. The results suggest that activation of PPAR γ ameliorates PCI via PPAR γ -NF- κ B as well as PPAR γ -STAT3 mediated deregulation of the cerebral inflammatory response. Further study assessing long-term outcomes and the exact mechanistic role of PPAR γ ; are warranted.

THE SPRINT TRIAL – INITIAL CLINICAL EVALUATION OF BOLUS CLEVIDIPINE FOR RAPID BLOOD PRESSURE MANAGEMENT IN CARDIAC SURGERY PATIENTS

Avery E; Brennan K; Aggarwal S; Streckenbach S; Donnelly A; Adams M; Cheung A

Massachusetts General Hospital Heart Center; University of Pennsylvania

Background: The ability to rapidly, reversibly and selectively decrease arterial blood pressure (BP) during cardiac surgery is important for managing events such as aortic cannulation and decannulation. Clevidipine (CLV) is a dihydropyridine calcium channel blocker and potent selective systemic arterial vasodilator. Because CLV is rapidly cleared with a half-life of approximately 1 minute, CLV intravenous (IV) bolus may provide a safe and effective means to rapidly control intraoperative BP. The SPRINT trial was performed to characterize the pharmacodynamic response to CLV IV bolus dosing.

Methods: This open-label, dose-ranging study assessed CLV administered as an IV bolus in patients 18 years undergoing cardiac surgery. Patients with a pre-anesthesia baseline systolic blood pressure (SBP) ≥ 140 mm Hg, in whom parenteral antihypertensive therapy was deemed necessary, were enrolled. A CLV bolus (given over <5 s) was administered prior to anesthesia at a dose of 0.125 mg, 0.25 mg or 0.5 mg. During surgery, a second CLV bolus could be administered immediately prior to aortic cannulation if necessary. BP (radial artery catheter) was recorded at baseline and every 5 sec after each bolus. The primary study endpoint was the mean maximum change in SBP from baseline after Bolus 1; secondary endpoints included time to maximum SBP change and time to 50% SBP recovery.

Results: Preliminary data for 27 of 31 enrolled patients (78% male, mean age 63 years) were analyzed. CLV Bolus 1 produced a dose-dependent decrease in SBP with a mean time to maximum response of 61 to 86 seconds and mean time to 50% recovery of 3.8 to 4.6 minutes (Table 1 and Figure 1). CLV Bolus 2 effectively decreased SBP for aortic cannulation. No patients required treatment for drug-induced hypotension after Bolus 1.

Conclusion: CLV IV bolus effectively and safely decreased BP with a predictable and brief duration of action in cardiac surgery patients. CLV IV bolus had a linear dose response over a dose range of 0.125 mg to 0.5 mg. The unique pharmacodynamic and pharmacokinetic properties of CLV IV bolus may be useful for achieving rapid and precise management of intraoperative BP upon demand during cardiac surgery.

THE USE OF AN ENDOTRACHEAL TUBE INTRODUCER IN A TRACHEAL RESECTION

Brandon M; Martinelli S; Feins R; Ben-Or S

University of North Carolina

A 65 year old male with right upper lobe lung carcinoma was taken to the operating room for a tracheal resection and pneumonectomy. During the conduct of the surgical procedure, stay sutures were placed on the left mainstem bronchus and distal trachea. The double lumen tube (DLT) was pulled back into the distal trachea, and the left main stem bronchus was divided. The left mainstem bronchus was intubated with a sterile armored 6.0 endotracheal tube (ETT) and ventilation resumed using a sterile circuit. The cuff on the DLT ruptured during the surgical dissection and was removed. A sterile 15 Fr, 70cm endotracheal tube introducer was advanced by the surgeon into the distal trachea and out the oropharynx. (Figure 1) An 8.0 ETT was passed over the endotracheal tube introducer but was not long enough to intubate the left mainstem bronchus. The endotracheal tube introducer was left in place and a 32 cm 6-0 cuffed Mallinckrodt Microlaryngeal Tracheal Tube (MLT) was advanced (Figure 2) past the anastomotic site under surgical visualization. The pneumonectomy and left mainstem anastomosis were completed and the MLT was withdrawn into the trachea. At the conclusion of the procedure, the patient was extubated without difficulty and taken to the recovery room.

To our knowledge, an endotracheal tube introducer has not previously been used on the surgical field to exchange an ETT during a carinal resection in this retrograde fashion. Pissonneault described the use of a sterile stylet through an indwelling ETT, secured on either side, in order to prevent accidental extubation during a tracheal resection¹. Sandberg reports the use of a red rubber catheter passed retrograde through the airway. An ETT is then sutured to the catheter and pulled into the airway by the surgeon².

During carinal resection, we recommend using a long sterile endotracheal tube introducer (a Cook 14 Fr 100cm soft-tipped extra-firm exchange catheter) passed retrograde into the pharynx for ETT exchange. This catheter allows the anesthesiologist to pass a DLT into the airway. The DLT has the necessary length to be easily placed distal to the surgical anastomosis.

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THE USE OF GLARGINE AS A BRIDGE FROM INSULIN INFUSION IN A DIABETIC AND NON-DIABETIC POPULATION AFTER CARDIAC SURGERY

Fermin L; Rhenman B; Bryning S; Dunn R

Southern Arizona VA Health Care System

OBJECTIVE: To compare the achievement of glucose control between a diabetic and a non-diabetic population after cardiac surgery using glargine to transition from a regular insulin infusion.

METHODS: Retrospective chart review of 99 consecutive patients that underwent cardiac surgery at our institution between July 2008 and February 2009. All patients received an intravenous regular insulin infusion according to our protocol postoperatively. The first 24 hours after surgery the glucose target was between 80-120 mg/dl. To transition from an insulin drip to glargine we calculated the 24 hours insulin requirement. Diabetic patients (preoperative glycosylated hemoglobin > 6.1) received 50% of this calculated dose, and non-diabetic patients (preoperative glycosylated hemoglobin < 6) received 25% of it. The insulin drip was turned down by half 2 hours after glargine was given, and discontinued 2 hours later. The target glucose value 48 hrs after surgery was < 200mg/dl.

RESULTS: Our population included 56 non-diabetic patients with glycosylated hemoglobin values = 5.77 [SPCHAR(plusmn)] 0.44; and 43 diabetics with glycosylated hemoglobin values = 7.2 [SPCHAR(plusmn)] 0.44. POD#1 at 06:00 glucose value in nondiabetics was 114.6 [SPCHAR(plusmn)] 22.75 and in diabetics was 123.69 [SPCHAR(plusmn)] 33. POD#2 at 06:00 glucose value in nondiabetics was 139 [SPCHAR(plusmn)] 22.46 and in diabetics was 163 [SPCHAR(plusmn)] 44.16. All the values represent mean [SPCHAR(plusmn)] standard deviation. None of our patients had a glucose < 80 mg/dl POD#2. Seven diabetics (16.2%) were above target POD#2, but only one non-diabetic (1.78%) was above target POD#2. The p value between our study populations glucose POD#2 using a two-tailed t test was < 0.005.

CONCLUSIONS Glargine is an easy and effective therapy to control serum glucose levels after open heart surgery even in patients with longstanding and poorly controlled diabetes. We plan to increase diabetics glargine dose to decrease glucose target levels POD#2.

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THE VALIDITY OF AN OXYGENATION INDEX FOR REFLECTING REPERFUSION INJURY IN CHILDREN UNDERGOING PULMONARY ARTERY BALLOONING

Yacouby S; Mossad E

Texas Children's Hospital

Introduction:

Balloon angioplasty of the pulmonary arteries is a common intervention performed in children with congenital heart disease (CHD) 1. The incidence and degree of lung reperfusion injury (RI) is not clear, and the method of diagnosis of such injury is variable 2. In this study, we investigated the validity of PaO₂:FiO₂ as an oxygenation index and marker for RI.

Methods:

With IRB approval, the records of children with a biventricular CHD undergoing pulmonary artery balloon angioplasty for a 2 year period were reviewed. Data collection included demographics, pre and post intervention hemodynamics, and arterial blood gas analysis. Markers of gas exchange were calculated using standard equations for A-aDO₂ and PaO₂:FiO₂ ratio 3. We examined the incidence of reperfusion injury, the distribution of PaO₂:FiO₂ post intervention, the relationship of clinical and laboratory manifestations of RI and the correlation between different oxygenation indices post intervention. Criteria for RI were based on the International Society of Heart and Lung Transplant (ISHLT) grading system 4. Additionally, the presence of pulmonary edema or hemorrhage, chest radiograph infiltrates served as clinical features of RI. Statistical analysis included T-Tests for continuous variables and Chi-square Fisher exact for categorical variables. A Pearson correlation coefficient was calculated to analyze the correlation between A-aDO₂ and PaO₂: FiO₂.

Results:

There were 46 patients identified in the study period. Patient age ranged from 2 months to 25 years (mean 6.2 +/- 6 years), weight ranged from 5 to 86 kg (mean 23 +/- 18 kg). RI was identified in 10/46 (22%) of the patients using clinical and ISHLT gas exchange criteria. The degree of RI was graded using the ISHLT criteria and correlated with clinical symptoms (p=0.002) (Table I). The PaO₂:FiO₂ ratio had a significant correlation to A-aDO₂ (r=-0.75) (Figure I) and a strong sensitivity (0.78) to identify patients with clinical RI (Table II).

Conclusion:

The PaO₂:FiO₂ oxygenation index is a sensitive test for identifying children with RI following pulmonary artery ballooning. Although not a specific test, the use of this index can confirm clinical suspicion and help guide decision making and care in the post-intervention period.

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THROMBOELASTOMETRY ROTEM® FOR MONITORING AND TREATING COAGULOPATHY IN CARDIAC SURGERY WITH DEEP HYPOTHERMIC CIRCULATORY ARREST DURING CARDIOPULMONARY BYPASS

Lee S; Lee J; Lee S; Sung K; Solomon C

Hannover Medical School; Samsung Medical Center, Sungkyunkwan University School of Medicine

Background: Our aim was to evaluate by means of ROTEM® the effect of deep hypothermic circulatory arrest (DHCA) on coagulation in patients undergoing on-pump cardiac surgery. We also assessed the predictability of fibrin-based ROTEM test FIBTEM before weaning from cardiopulmonary bypass (CPB) for cryoprecipitate requirement after CPB to correct bleeding diathesis.

Methods: Ten patients undergoing cardiac surgery involving CPB with DHCA (DHCA group) and eight without DHCA (CPB group) were enrolled. Blood was sampled before incision (Baseline), 30' before CPB weaning (Cweaning), and 5' after protamine reversal (Preversal). Standard coagulation parameter and following ROTEM parameters were recorded: clot formation time (CFT), alpha angle, clot amplitude A10, maximum clot firmness (MCF) and maximum clot elasticity (MCE) in extrinsically-activated test EXTEM and FIBTEM. MCEplatelet, the platelet component of clot strength, was calculated using $MCE_{EXTEM} - MCE_{FIBTEM}$. The predicted value of FIBTEM A10 during CPB for cryoprecipitate transfusion at Preversal was calculated. Cryoprecipitate was administered when FIBTEM A10 at Preversal \leq 5 mm.

Results: Demographic and baseline data were similar between the groups. At Preversal, EXTEM CFT, alpha angle and A10 reflected more compromised coagulation in DHCA group compared to CPB group (P 0.04, 0.02, and 0.03). FIBTEM A10 at Cweaning and Preversal were also significantly lower in DHCA group (P 0.003, and 0.03, respectively; median, minimum, maximum at Cweaning and Preversal 11, 8, 18mm and 12, 8, 18mm in CPB group, 3, 2, 9mm and 5, 3, 15mm in DHCA group). Although platelet counts were comparable between the groups (median, minimum, maximum = 82.5, 35, 138×10^3 /mm³ in CPB group, 63.5, 44, 138×10^3 /mm³ in DHCA group), MCEplatelet at Preversal was significantly lower in DHCA group (P 0.026). In contrast, both fibrinogen and MCEFIBTEM at Preversal were significantly lower in DHCA group (P 0.02 for both). The correlation between MCEFIBTEM and fibrinogen was r^2 0.73 for CPB group and r^2 0.6 for DHCA group.

The cut-off points for A10 and MCF of EXTEM to reflect platelet count of 100×10^3 /mm³ were 45mm, 48mm. FIBTEM at Preversal to reflect 200 mg/dl of fibrinogen were 5mm, 6mm respectively. FIBTEM A10 at Preversal was related to Cweaning as follows: $FIBTEM_{A10} \text{ at Preversal} = 2.34 + 0.93 \times FIBTEM_{A10} \text{ at Cweaning}$. Using this equation, the cut-off value for FIBTEM A10 at Cweaning to best reflect 200 mg/dl of fibrinogen was 3mm. Positive and negative predictive values for FIBTEM A10 \leq 3mm vs. $>$ 3mm at Cweaning for need of cryoprecipitate transfusion at Preversal (FIBTEM A10 at Preversal \leq 5 mm) were 100% and 91.7%, respectively.

Conclusion: ROTEM® was useful for evaluating coagulation abnormalities after DHCA and for optimally preparing cryoprecipitate in advance. DHCA group showed overall greater coagulation defects, and significantly lower fibrinogen level appeared to be an important factor to affect clot strength after weaning from pump, compared to CPB group. This aspect needs to be considered when managing the patients with bleeding risk.

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TIMING OF RBC TRANSFUSION ON ACUTE KIDNEY INJURY IN CARDIAC SURGERY

Hathaway J; Welsby I; Stafford-Smith M; Phillips-Bute B; Gaca J; Swaminathan M; Shaw A; Hill S

Duke University Medical Center

Introduction – In cardiac surgery, acute kidney injury (AKI) is common and thought to be mediated by ischemia, to which the kidneys are prone [1]. In the same patient population, RBC transfusion has been independently associated with AKI [2]. Here, ischemia also seems a likely mechanism for AKI from a host of well described changes that occur during the storage of blood, including: depletion of 2,3-DPG, increased adhesion and aggregation, decreased levels of NO, accumulation of inflammatory mediators, and decreased deformability leading the impairment of microvascular flow, collectively referred to as storage lesion [3]. The lungs are the first organ in contact with transfused blood, and when considering allocation of cardiac output and extensive microvasculature, would seem to expend much of this storage lesion burden. When the lungs are bypassed, these effects should be directed to the systemic circulation, and hence increase this ischemic effect on the kidneys. Therefore, our hypothesis asked if this preferential systemic distribution that occurs on CPB is clinically significant, meaning is the AKI measurably greater when the lungs are bypassed?

Methods and Results – With IRB approval, perfusion records were obtained and matched to database records from those patients receiving single unit RBC transfusions for CABG only from 1996-2005. Of the 411 single unit transfusion procedures examined, 77 (19%) were transfused on bypass and 334 (81%) were transfused off bypass. To examine the association between time of transfusion and renal outcome, we constructed a multivariable linear regression model. The outcome is % delta creatinine, calculated as $((\text{max postop cr} - \text{preop cr})/\text{preop cr}) * 100$. The primary predictor of interest is timing of transfusion. Also considered in the model as covariates were age, weight, preoperative creatinine, and gender. These covariates were chosen based on previous research, which indicates that they are associated with % delta creatinine. No association was detected between timing of transfusion and % delta creatinine after adjusting for covariates [26.27(38.48) vs 25.76(37.62), $p=0.92$].

Conclusion – In single RBC unit recipients, we were unable to detect a difference in AKI after cardiac surgery based on the timing of RBC transfusion.

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TRANSCEREBRAL METABOLOMIC PROFILING OF COGNITIVE DECLINE AFTER CARDIAC SURGERY

Chen C; Podgoreanu M; Mackensen G; Stafford-Smith M; White W; Newman M; Mathew J

Duke University Medical Center

Introduction: Neurocognitive impairment occurs frequently in the large number of increasingly elderly patients undergoing cardiac operations every year. Recently, metabolomic profiling has enabled comprehensive analyses of changes in metabolic fuel selection in a variety of models, including cardioplegic arrest. We hypothesized that patients with postoperative cognitive deficit would be associated with a different transcerebral metabolomic profile than those without a deficit.

Methods: After IRB approval and informed consent, 10 patients undergoing CABG, Valve, or CABG + Valve surgery with cardiopulmonary bypass were enrolled. Patients were excluded if they had a history of symptomatic cerebrovascular disease, psychiatric illness, creatinine >2 mg/dL, <7th grade education, or had a Mini Mental State Examination score <24. Each patient had a radial artery catheter placed and a 16G 5.25-inch catheter inserted retrograde into the right internal jugular vein. Paired arterial and jugular vein blood samples were collected simultaneously into EDTA- and protease inhibitor-treated tubes at baseline, 10 minutes after removal of cross-clamp (AXC), and end of surgery. Plasma concentrations of metabolites representing the amino acid, carbohydrate, energy, lipid, and nucleotide pathways were assessed using gas and liquid chromatography mass spectrometer platforms. Patients were also evaluated with a well-validated battery of 5 cognitive tests at baseline and 6 weeks after surgery. Test scores were subjected to factor analysis to calculate the cognitive deficit rate. The difference between metabolite extraction ratios (jugular-arterial/arterial) at baseline and 10 minutes after AXC removal was assessed in patients with and without cognitive deficit using a paired t-test; $p < 0.05$ was considered significant.

Results: Of the 10 patients, 3 were female and 5 underwent CABG surgery, 1 had CABG [SPCHAR(plusmn)] valve surgery, and 4 had valve surgery. The mean age was 62 [SPCHAR(plusmn)] 13.6 and the cognitive deficit rate was 40%. Significant differences in metabolite extraction between baseline and 10 minutes after AXC were detected in the lipid, amino acid, and nucleotide pathways (Table).

Conclusions: Transcerebral metabolomic profiling can successfully identify differences in patients experiencing cognitive deficit after cardiac surgery. Elevated lipid levels have been shown to be markers for acute demyelination and may be partly associated with postoperative cognitive decline.

TRANSESOPHAGEAL 3D ECHOCARDIOGRAPHY IS SUPERIOR TO 2D ECHOCARDIOGRAPHY FOR MEASUREMENT OF PROSTHETIC AORTIC VALVE EFFECTIVE ORIFICE AREA

Greenberg J; Shook D; Andrawes M; Novak T; Shernan S

Brigham and Women's Hospital

Background: Prosthetic valve mismatch has been reported in up to 50% of patients after aortic valve replacement (AVR), and is an independent predictor of mortality¹. Typically, echo-derived AVR effective orifice area (EOA) is derived from the continuity equation by calculating left ventricular outflow tract area (ALVOT) from its diameter using two dimensional (2D) views, and assuming the ALVOT is a circle. However, this method may provide erroneous values since the LVOT can often be elliptical or irregularly shaped. We aim to compare the accuracy of conventional 2D versus three dimensional (3D) echo measurements of prosthetic AVR EOA, by comparing these with the gold standard values provided by the manufacturer.

Methods: Following CPB and chest closure, EOA was derived from the continuity equation using TEE-acquired measurements in 5 patients undergoing AVR. LVOT diameter was first measured at the 2D midesophageal AV long axis view. Area was calculated using standard assumptions that the LVOT is a circle. Next, LVOT was measured from short axis views derived from 3D TEE full volume data sets (IE33, Matrix; Philips Healthcare, Inc.) from two perpendicular diameters assuming an elliptical shape (3DE), and subsequently by direct planimetry (3DP) (Figure). LVOT and AV velocity time integrals were obtained with pulse- and continuous-wave doppler respectively. AVR EOAs were then calculated using the continuity equation for both 2D and 3D TEE ALVOT measurement techniques.

Results: All 5 patients underwent bioprosthetic AVR. Mean EOA values were $1.45 \pm 0.46 \text{ cm}^2$, $1.89 \pm 0.61 \text{ cm}^2$ and $1.92 \pm 0.63 \text{ cm}^2$ respectively for the 2D, 3DE and 3DP techniques (Table 1). The mean in-vitro EOA (gold standard) acquired from the manufacturers was $2.18 \pm 0.72 \text{ cm}^2$. A pairwise comparison of the mean EOAs acquired via the 2D TEE techniques versus the in-vitro gold-standard values revealed a significant 34% underestimation, while a similar comparison revealed no significant difference between either 3D TEE technique vs the gold standard values for AVR EOA.

Discussion: LVOT asymmetry may result in underestimation of AVR EOA calculated from the continuity equation, when conventional 2D echo techniques are used to measure ALVOT. Errors in calculated ALVOT measurements can have important clinical implications, and may account for overestimated reports of prosthetic valve stenosis. Alternatively, 3D TEE allows direct measurements of ALVOT with fewer geometric assumptions, and thus permits more accurate calculations of AVR EOA.

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TRANSESOPHAGEAL ECHOCARDIOGRAPHY MONITORING DECREASES MORBIDITY AND MORTALITY IN PATIENTS WITH RENAL CELL CARCINOMA WITH CAVAL THROMBUS

Rumjahn H; Roffey P; Roby J; Mogos M; Thangathurai D

Keck School of Medicine

Introduction. It is not uncommon for renal cell carcinomas to invade the inferior vena cava (IVC) and extend into the hepatic vein and the right atrium. This is a fatal condition unless operated on as an urgent procedure. The surgery and anesthetic management is challenging due to the risk of embolism, hypotension, and bleeding. For the last five years, we have used intraoperative transesophageal echocardiography (TEE) in these cases and have found it useful for monitoring and detecting any potential intraoperative complications as well as assessing complete removal of the thrombus.

Materials and Methods. The data was obtained using our institution's Urology Department data bank, collected over a 25-year period. Over 250 total cases of this type were performed over this time period. For the last five years, there were 30 cases where TEE was used. These patients had a thrombus Level I (intrahepatic), II (intrahepatic), or III (extending into the right atrium). TEE was an important aspect of the management of these patients. The patients all had large bore introducers placed in the internal jugular veins bilaterally using a high approach. Pulmonary artery catheter use was contraindicated due to the risk of breaking the thrombus and causing embolization. The thrombus was monitored throughout the surgery via TEE.

The TEE aided in volume status assessment, which was otherwise difficult to monitor due to the risks associated with placing a PA catheter. It also helped assess venous return which is affected by the thrombus and the intraoperative clamping of the IVC. Ten percent of the cases had significant atrial extension of the thrombus that required the patient to be placed on cardiopulmonary bypass for 5-10 minutes. Blood loss varied from 3 liters to 25 liters. After tumor and thrombus removal, the TEE was used to monitor for any residual thrombus in the IVC, hepatic vein, and atrium. Pulmonary outflow tracts and the right ventricle were also assessed for any emboli. In the postoperative period, TEE was also useful in excluding any new thrombus formation in the hepatic vein and IVC. In spite of massive blood loss, none of the patients developed any significant respiratory, renal, or cardiac complications. Overall, the mortality in these patients was reduced by 20% compared to those who did not receive TEE monitoring.

Conclusion

TEE is useful in patients with renal cell carcinoma with IVC thrombus to detect early thrombus embolization and to aid in assessment of volume status. At the end of surgery, it allows visualization of the IVC, hepatic vein, and atrium for residual thrombus, as well as any embolization to the right ventricle or pulmonary artery.

TRANSLATIONAL APPROACH TO IDENTIFYING CARDIOPROTECTIVE EFFICACY OF A NOVEL ANNEXIN-A1 TRIPEPTIDE IN THE SETTING OF ISCHEMIA-REPERFUSION

Ma Q; Zhang Z; Machensen G; Podgoreanu M

Duke University Medical Center

Background: Perioperative myocardial injury (PMI) due to ischemia/reperfusion (I/R) remains a major cause of cardiovascular morbidity and mortality following cardiac surgery, yet identification of effective cardioprotective compounds has proven difficult due to a number of barriers at the preclinical level. We tested the cardioprotective efficacy of a novel Annexin-A1 mimetic tripeptide (ANXA1sp) in vitro using a two-state adult rat ventricular cardiomyocyte (ARVC) model of simulated ischemia-reperfusion under both normo- and hyperglycemic conditions, and validated our findings in vivo using a rodent model of cardioplegic arrest (CA).

Methods: In vitro study: adult ventricular cardiomyocytes (AVC) from male SD rats were incubated in normal or high glucose (25mM), with and without 30 μM ANXA1sp, respectively for 24 h. Cells were subjected to 2h oxygen-glucose deprivation (OGD), followed 24h reoxygenation in either normo- or hyperglycemic conditions. Cell death was determined histologically (trypan blue exclusion) and biochemically (supernatant levels of cardiac troponin I – cTnI and heart-type fatty acid binding protein – hFABP, ELISA). Apoptosis was quantified using ELISA. In vivo study: with IACUC approval, male SD rats were randomly assigned to 4 groups in a 2x2 design (n=3/group): normoglycemic and hyperglycemic cardioplegic arrest (CA), each treated with ANXA1sp or vehicle, respectively. All animals underwent 75 min of moderate hypothermic CPB with 45 min of CA using blood cardioplegia. Treatment groups received ANXA1sp (1mg/kg) before (ip), during (with cardioplegia), and after CPB (ip), whereas CA control animals received saline. No animals received insulin. At 24 h after CPB animals were sacrificed and myocardial apoptosis quantified using both activated caspase-3 (Immunostaining) and TUNEL assays. Myocardial necrosis was quantified as plasma levels of cTnI and hFABP (ELISA).

Results: Acute hyperglycemia directly increased myocardial injury following I/R both in vitro (in the absence of leukocyte-endothelial interactions) and in vivo. ANXA1sp significantly attenuated myocardial I/R injury under both normo- and hyperglycemic conditions, as confirmed by significantly decreased myocardial necrosis (cTnI and hFABP), caspase-3 activity, and number of apoptotic myocardial cells (Table).

Conclusions: We used a translational approach to provide preclinical evidence that ANXA1sp significantly attenuates myocardial injury following I/R under both normoglycemic and hyperglycemic conditions. The cardioprotective effects of ANXA1sp include reduced myonecrosis and apoptosis, as well as inhibition of pro-inflammatory pathways. Integrated systems approaches to test efficacy of novel cardioprotective compounds at cellular and whole organ level in clinically relevant animal models are necessary to identify robust perioperative organ protective strategies.

TREATING CARDIAC SURGERY PATIENTS FOR HEPARIN-INDUCED THROMBOCYTOPENIA BASED ON EASILY AVAILABLE ELISA RESULTS

Manji R; Bell D; Loong-Saw C; Nickerson P; Moltzan C; Menkis A; Jacobsohn E

Canadian Blood Services; Cardiac Sciences Program, University of Manitoba; University of Manitoba

Background: Heparin induced thrombocytopenia (HIT) and thrombosis (HITT) are devastating problems with significant morbidity, mortality, cost and litigation potential. Currently, the best test to determine if a patient has HIT is a functional platelet assay (eg.the serotonin release assay (SRA)); however this test is not widely available. Most centers do have access to an ELISA which detects the anti-platelet factor 4-heparin antibody (HIT antibody); however, this test is associated with high false positive rates (especially in a cardiac surgery patient). If one suspects HIT, one needs to anticoagulate with often expensive non-heparin anticoagulants which pose their own risks of bleeding (especially post cardiac surgery) and may be difficult to reverse. If the association between ELISA result (in optical density – OD units) and the likelihood of a positive SRA is known, then a patient care algorithm could be developed.

Objectives: To review ELISA OD readings and SRA results (as the current gold standard) in a cardiac surgery population to determine the association, and to potentially devise an algorithm for care at the bedside.

Methods: The results of ELISA OD were compared to patients with an SRA result. The ELISA kit used was a commercial EIA from GTI Inc. The SRA were done at McMaster University, Hamilton, Ontario. A positive ELISA was an OD value greater than or equal to 0.4.

Results: There were 139 cardiac surgery patients who had an ELISA done due to clinical suspicion of HIT. Of these 139, 17% (23 patients) had an ELISA ≥ 0.4 and thus had confirmation by SRA of which 26% (6 patients) were positive. The ELISA OD (mean +/- SEM) of the confirmed SRA positive cases (n=6) was 2.379 +/- 0.2246 and that for the confirmed SRA negative cases (n=17) was 0.8275 +/- 0.1417 (p<0.001). An ROC curve was created which gave an area under the curve of 95.1% (p=0.001). The table shows the various cutpoints. Using an ELISA OD of 1.3695 gave a sensitivity of 100%, a specificity of 94.1%, a positive predictive value of 85.7% a negative predictive value of 100%, a positive likelihood ratio of 16.9 and a negative likelihood ratio of 0.

Conclusions: Our data suggest that one should treat patients for HIT using an alternative to heparin agent (such as fondaparinux) if they have an ELISA OD value of 1.3695 or greater. The ELISA test can be done in most institutions with a result available the same day as the test is done. Using this cut off may balance the benefits and risks of treating HIT with an alternative to heparin agent.

UNEXPECTED COMPLICATIONS WITH SPRAY CRYO-THERAPY FOR OBSTRUCTING AIRWAY TUMORS.

Pedoto A; Amar D; Desiderio D; Finley D

Memorial Sloan Kettering Cancer Center; Memorial Sloan-Kettering Cancer Center

Introduction: Few options exist for patients with advanced airway tumors. Spray cryo-therapy (SCT) is a novel method that uses non-contact delivery of liquid nitrogen at 2-4 psi and -196[SPCHAR(deg)] C, via a catheter through an endoscope, causing rapid freezing and thawing of tissue with cellular death and hemostasis (1). This technique has been used primarily to ablate abnormal esophageal tissue (2); however, limited data are available on its effects on airway tumors (3). We reviewed our first experience of SCT for the treatment of obstructing airway tumors and associated complications.

Methods: SCT was performed on 22 patients with symptomatic primary or metastatic airway tumors with limited options for other treatment. A minimum of 3 cycles of 5 seconds each were administered to each patient, with a complete visual thaw between each cycle. All patients underwent general anesthesia for combined rigid and flexible bronchoscopy. Most of the patients had intra-arterial blood pressure monitoring and all perioperative events were recorded.

Results: A total of 24 treatments were performed in 22 patients whose median age was 60 years (range 15-88 yr). Nearly half of the tumors were primary lung cancer, with the remaining being metastatic lesions: 21 tumors were located distal to the carina and 14 were > 90% occlusive. The median procedure length was 60 min (range 15-153 min). 54% of the cases were outpatients, 37% inpatients and 16% required overnight admission due to complications. Ten patients had serious intraoperative events listed in table 1 and of these, three cases required reintubation and mechanical ventilation overnight, and one patient suffered a cardiac arrest and died in the operating room.

Conclusions: SCT is a novel method of re-establishing airway patency in case of symptomatic airway tumors. In our early experience, SCT was associated with unexpected and serious respiratory or cardiovascular compromise. While this technique may offer advantages over airway laser therapy such as no risk for fire or improved hemostasis, further study is needed for better patient selection and improved safety.

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URINARY NGAL AND ADVERSE OUTCOMES FOLLOWING ADULT CARDIAC SURGERY: LOOKING BEYOND CREATININE

McIlroy D; Wagener G; Wang S; Lee H

Columbia University College of Physicians and Surgeons

Background: Acute kidney injury (AKI) is a frequent complication following cardiac surgery and an independent predictor of postoperative morbidity and mortality (1). Serum creatinine, the current diagnostic standard for AKI, is both insensitive and slow to rise in response to acute injury, limiting the possibility for early diagnosis and targeted intervention (2). Consequently, new biomarkers permitting early diagnosis of AKI are desperately required. Urinary NGAL is a novel biomarker of renal injury, although its diagnostic performance for AKI following adult cardiac surgery appears modest (3). However, due to creatinine's own limited sensitivity for acute kidney injury, its use as the diagnostic reference standard for new biomarkers may produce incorrect estimates of performance (4). We therefore sought to investigate the association between urinary NGAL and clinically relevant adverse outcomes following adult cardiac surgery. We hypothesized that increasing urinary NGAL in the early postoperative period would be associated with increased mortality or need for dialysis, as well as increased hospital length of stay (hLOS). **Methods:** Following IRB approval, we performed a prospective study in 417 adult cardiac surgical patients. Preoperative renal replacement therapy was the only exclusion criteria. Urinary NGAL was determined serially by ELISA, commencing preoperatively and continued 18-hours postoperatively. The primary outcome was the composite of in-hospital mortality or renal replacement therapy with hLOS a secondary outcome. Receiver operator characteristic curves were used to determine optimal threshold values for NGAL. Regression analyses determined the association between NGAL and both the primary composite outcome and hLOS.

Results: The primary outcome occurred in 16 patients. Within 3 hours of cardiopulmonary bypass (CPB) an elevated NGAL was associated with a 4.1-fold increase in odds for in-hospital mortality or renal replacement therapy (95% C.I. 1.1-15.2, $p=0.03$) and independently associated with a 19% increase in hLOS (95% C.I. 1.10-1.30, $p=0.0001$) despite adjusting for age, gender, Parsonnet score, preoperative creatinine clearance, reoperative status and body mass index.

Conclusions: Urinary NGAL in the early post-CPB period is associated with increased morbidity and mortality following adult cardiac surgery and independently associated with increased hLOS potentially reflecting acute kidney injury. This provides important evidence supporting the validity of NGAL as an early marker of clinically significant renal injury following adult cardiac surgery.

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USING THE VALSALVA MANEUVER AND ANALYSIS OF HEART RATE AND BLOOD PRESSURE VARIABILITY TO IDENTIFY PATIENTS WITH AUTONOMIC DYSFUNCTION PRIOR TO CARDIAC SURGERY

Deschamps A; Couture P; Rochon A; Lebon J; Ayoub C; Qizilbash B; Cogan J; Toledano K; Pagé P; D'Antono B; Denault A

Montreal Heart Institute; Montreal Heart Institute, University of Montreal

Introduction: Autonomic dysfunction is common in cardiac patients and may affect perioperative outcome of cardiac surgery with cardiopulmonary bypass. Identification of patients with baseline autonomic dysfunction or with an abnormal response to autonomic challenges could prevent complications of cardiac surgery. However, bedside testing of autonomic dysfunction and its relationship to perioperative outcome has not been described. To diagnose patients with baseline autonomic dysfunction we used analysis of heart rate (HRV) and blood pressure (BPV) variability at rest. To diagnose an abnormal response to autonomic challenges we used analysis of HRV and BPV while the patients performed the Valsalva maneuver to stimulate the autonomic nervous system.¹

Methods: After informed consent was obtained, an ECG, continuous non-invasive blood pressure (BP) and respiratory rate was measured at rest for 15 min. The patients were then asked to perform a Valsalva maneuver for 15 sec. and the measurements were repeated for another 15 min. The data was saved on a portable computer at a sampling rate of 1000 Hz. Extraction of the R-R intervals from the ECG and of the beat-to-beat values of BP was achieved with an automated commercial software with appropriate corrections for ectopic beats. The analysis of HRV and BPV was obtained using wavelet transformation, a technique that allows the extraction of non-stationary signals. Demographic data and perioperative risk estimation (Parsonnet score) were obtained from the charts. An abnormal Valsalva response was defined from previously accepted criteria.¹

Results: Of 67 patients studied, 38 (56.7%) had a normal response to the Valsalva maneuver and 29 (43%) had an abnormal response. Gender, age, Parsonnet scores, cardiac failure, diabetes and hypertension did not differ between the groups. Baseline HRV was different between the groups, 18,764 +/- 3,505 (SE) msec² for the normal response versus 73,386 +/- 27,158 msec² for the abnormal response (p=0.0116, Mann-Whitney). In patients with a normal response, HRV values increased significantly after the Valsalva maneuver and returned to baseline thereafter. In patients with an abnormal response there was no increase HRV and the values remained significantly higher than in the other group. BPV values did not differ at baseline nor did they differ with the Valsalva maneuver.

Discussion: Autonomic dysfunction is common in cardiac surgery patients. More than 40% of patients have an increase in baseline HRV (parasympathetic tone). These patients also have an abnormal response to the Valsalva maneuver and seem limited in their capacity to increase parasympathetic activity. Gender, age, Parsonnet scores, cardiac failure, diabetes, hypertension and BPV did help to differentiate the patients. HRV could therefore be used to identify cardiac surgery patients with autonomic dysfunction that could be confirmed by an abnormal response to the Valsalva maneuver. Whether these patients are more at risk for perioperative complications needs to be investigated.

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