SCA13

DOES PROPHYLACTIC ADMINISTRATION OF SIVELESTAT SODIUM HYDRATE IMPROVE POSTOPERATIVE PAO2/FIO2 RATIO IN PATIENTS UNDERGOING CARDIAC AND AORTIC SURGERY WITH CARDIOPULMONARY BYPASS?

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Background: Cardiopulmonary bypass (CPB) causes systemic inflammatory response syndrome that often leads to acute lung injury (ALI). Several studies have suggested that the earlier administration of Sivelestat sodium hydrate (SSH) inhibits the increase of neutrophil elastase activity in patients of ALI an decreases morbidity and mortality. However, little has been reported on prophylactic administration of SSH to patients undergoing cardiac and aortic surgery with CPB.

The purpose of this study was to assess whether prophylactic administration of SSH improves postoperative PaO2/FIO2 ratio in patients undergoing cardiac and aortic surgery with CPB.

Methods: The Institutional Review Board of Kanagawa Cardiovascular and Respiratory Center approved this study. Between July 2005 and June 2007, 40 patients scheduled for elective cardiac valve repair or thoracic aortic surgery with CPB were allocated to two groups: receiving SSH 0.2mg /kg/h (group S, n = 20) or normal saline 0.1ml/kg/h (Control: group C, n = 20). SSH or normal saline infusion was started after the induction of anesthesia, and was continued for 24 hours. Activity of neutrophil elastase and interleukin-8, white blood cell count, C-reactive protein, and PaO2/FIO2 ratio were measured until as long as the 3rd postoperative day. Artificial ventilation time and the duration of ICU stay were also documented. Values are shown as mean ±; S.D. Comparisons were made with the Students unpaired t-test or chi-square test when appropriate, and values of $p < 0.05$ were considered significant.

Results: Five patients were excluded because of failed weaning from CPB, massive bleeding, reoperation and perioperative heart failure. Thirty-five patients were finally included to the study (18 in group S, 17 in group C). Patient characteristics showed no statistical difference in age, gender, weight, the operation time and the CPB time. Activity of neutrophil elastase was significantly lower in group S compared with group C, at immediate after ICU admission, and on 1st postoperative day (group S vs. group C: 0.73 ± 0.95 mM/L vs. 4.29 ± 6.40 mM/L; $P < 0.03$, 0.01 ± 0.03 mM/L vs. 0.21 ± 0.31 mM/L; $P < 0.01$, respectively).

No difference was seen between two groups in interleukin-8, white blood cell count, C-reactive protein, PaO2/FIO2 ratio, artificial ventilation time, and the duration of ICU stay. Complications that derived from SSH were not observed.

Conclusion: Although prophylactic administration of SSH significantly suppressed activity of neutrophil elastase, improvement of postoperative PaO2/FIO2 ratio was not clear in the patients underwent cardiac and aortic surgery with CPB.

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SCA14

PLATELET TRANSFUSION IN CARDIAC SURGERY DOES NOT CONFER INCREASED RISK FOR ADVERSE MORBID OUTCOMES

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Background

Perioperative platelet transfusion has been reported to confer increased morbidity following cardiac surgery but prior studies were limited by confounding variables including concomitant red blood cell (RBC) transfusions. Our objective was to examine the impact of platelet transfusion on adverse outcomes in cardiac surgery controlling for patient, operative, and perioperative transfusion-related variables.

Methods

32,298 patients underwent isolated coronary artery bypass grafting (CABG), an isolated valve, or a combined CABG and valve procedure requiring cardiopulmonary bypass (CPB) between 01/01/1993 and 01/01/2006. Propensity methodology was employed to assess the association between platelet transfusion and adverse morbid outcomes.

Results

Prior to risk adjustment, platelet transfusion conferred increased morbidity and mortality. Propensity methods yielded 2,774 matched-pairs by platelet transfusion status. Among propensity-matched pairs, platelet transfusion was associated with similar or reduced morbid outcomes, platelet vs. no platelet transfusion: cardiac 2.42% vs 1.77%, P=0.09; pulmonary 8.94% vs 9.88%, P=0.23; renal 1.33% vs 1.48%, P=0.65; neurologic 2.27% vs 3.21%, P=0.033; serious infection 4.15% vs 5.34%, P=0.037; hospital mortality 2.05% vs 3.06%, P=0.017; and composite morbid outcome 15.0% vs 17.2%, P=0.024, respectively.

Conclusion

Transfusion of platelet concentrates in the perioperative period is not associated with increased morbid outcomes or in-hospital mortality following cardiac surgery. Furthermore, platelet transfusion may even confer benefits relative to reduced morbid outcomes.

SCA15

STATINS ARE INDEPENDENTLY ASSOCIATED WITH REDUCED MORTALITY IN PATIENTS WITH PREOPERATIVE RENAL INSUFFICIENCY UNDERGOING CORONARY ARTERY BYPASS GRAFT SURGERY

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Background: Preoperative statin therapy has been reported to be associated with reduced mortality and morbidity after cardiac and noncardiac surgery. Recently, preoperative statin therapy was shown to be significantly associated with a reduced incidence of new onset postoperative renal insufficiency (RI). We investigated if preoperative statin therapy reduces postoperative morbidity and mortality in patients with preoperative RI undergoing primary coronary artery bypass graft surgery (CABG) with cardiopulmonary bypass (CPB).

Methods: A retrospective cohort study was performed of 3632 consecutive patients undergoing primary CABG surgery with CPB between January 2002 and June 2007. Patients with preoperative RI (n=641) and normal renal function (n=2991) were further subdivided into two groups: patients receiving preoperative statin therapy and patients not receiving preoperative statin therapy. Multivariate logistic regression analysis was performed controlling for patient demographics, perioperative risk factors and medications to determine if preoperative statin therapy is an independent predictor of reduced postoperative mortality and morbidity (e.g., ventilator dependence, arrhythmias, cardiac arrest, RI, stroke, myocardial infarction, bleeding requiring reoperation, sternal wound infection, and sepsis). Multivariate linear regression analysis was also performed for a continuous variable of hospital stay.

Results: Multivariate analysis revealed that preoperative statin therapy was independently associated with a significant reduction in 30-day all-cause mortality (9.96 % versus 5.0%, $p < 0.01$) and hospital stay (16.8 ± 17.6 days versus 15.0 ± 13.2 days, $p<0.01$) in patients with preoperative RI undergoing CABG surgery.

The risk-adjusted odds ratio (OR) for reduction of the mortality in patients receiving preoperative statin therapy compared with patients not receiving preoperative statin therapy was 0.485 (95% confidence interval [CI] = 0.25-0.93). Moreover, preoperative statin therapy was independently associated with reduction in postoperative RI (9.7% versus 6.2%; OR = 0.60; 95% CI = 0.45-0.80; $p<0.01$) and hospital stay (11.6 ± 10.5 days versus 9.8 ± 6.3 days; $p<0.01$) in patients with normal preoperative renal function undergoing CABG surgery.

Conclusion: Preoperative statin therapy is an indepenedent predictor of reduced mortality after primary CABG surgery in patients with preoperative RI. Furthermore, these data suggest that the postoperative renoprotective effects of statin therapy in patients with normal preoperative renal function may in part explain the observed reduction in postoperative mortality in patients with preoperative RI undergoing CABG surgery.

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SCA16

MOLECULAR CLASSIFICATION AND PREDICTION OF MULTIPLE ORGAN FAILURE COMPLICATING CARDIAC SURGERY USING MULTIPLEX SERUM PROTEIN MARKERS

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Introduction: Cardiac surgery with cardiopulmonary bypass (CPB) induces robust activation of systemic host responses to injury, implicated in the pathogenesis of multiple organ dysfunction syndrome (MODS).

With an incidence of up to 11%,1 MODS is the major cause of late in-hospital mortality (41%)1 and increased resource utilization following cardiac surgery,2 yet remains poorly predicted by current risk stratification algorithms.3 We hypothesized that the pathological processes leading to postoperative MODS would cause characteristic changes in the concentrations of serum signaling proteins, resulting in a detectable MODS-specific molecular phenotype.

Methods: The Sequential Organ Failure Assessment (SOFA) score was calculated daily until intensive care unit discharge or for a maximum of 5 postoperative days. MODS was defined as a SOFA score ≥;2 in more than one organ system on postoperative day 3 and onward.4 MODS patients (n=10) were matched to non-MODS controls (n=10) on 4 background covariates (EuroSCORE, CPB time, insulin dependency and date of surgery) previously selected in a stepwise parsimonious logistic regression model developed in n=948 patients. Concentrations of 34 cytokines, chemokines, angiogenesis/growth factors, and soluble receptors were simultaneously measured in duplicate in serum samples obtained at baseline and postoperative day 1 using multiplex immunobead assay technology (Bioplex, BioRad, Hercules, CA).

Significance analysis of microarrays (SAM)5 was employed to identify differentially expressed proteins between MODS and control patients, followed by predictive analysis of microarrays (PAM)6 with five-fold cross-validation to generate and internally validate a MODS-specific protein signature.

Results: SAM identified 10 proteins (IL-1β;, IL-6, IL-8, IL-18, IP-10, TNF-α;, MCP-1, G-CSF, tPAI-1 and sFasL) with highly significant differences in expression ($p<0.003$) between MODS and control patients on postoperative day 1. Furthermore, in PAM analyses these 10 proteins were globally predictive of MODS occurrence on postoperative day 3 with 88% positive agreement and 81% negative agreement. Interestingly, preoperative levels of 2 proteins (MIF and RANTES) were also significantly different between MODS and control patients.

Conclusion: In this preliminary analysis, we report on the use of a targeted proteomic approach by multiplex immunoassays to identify distinct candidate serum biomarkers profiles predictive of multiple organ failure following cardiac surgery with CPB, independent of known clinical and procedural risk factors. Although the dynamic perioperative changes in serum signaling proteins seem most informative for MODS prediction, the observed differences in baseline concentrations may reflect altered genetic susceptibilities for a proinflammatory state and thus be potentially useful in preoperative risk stratification.

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SCA17

A RANDOMISED CONTROLLED TRIAL OF CELL SALVAGE IN ROUTINE CARDIAC SURGERY

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Objectives:

To determine whether cell salvage for cardiac surgery reduces blood transfusion and is cost- effective, in the setting of a rigorous transfusion protocol and routine administration of anti-fibrinolytics.

Design:
Randomised controlled trial.

Setting:
Single centre study at a specialist cardiothoracic surgery hospital in the UK.

Participants:
325 patients presenting for first-time cardiac surgery (including CABG, valve or combined surgery) were assessed for entry into the trial and 213 were finally included and randomised after informed consent.

Interventions:
Patients randomised to control or cell salvage; the latter had all blood lost in theatre and critical care (first 6 hours) processed and auto-transfused. All patients received tranexamic acid.

Outcome measures:
The primary outcome was any exposure to allogeneic blood products regardless of amount. Secondary outcomes were the number of units of red blood cells, FFP or platelets transfused; cost analysis and safety was also examined.

Results:
There was no significant difference between the two groups (table 1) in the proportion of patients exposed to allogeneic blood (32% in both groups, relative rate 1.0 p=0.89). At current blood products and cell saver prices in the United Kingdom, cell salvage is more expensive by a minimum of £67 (sterling) per patient. When patients who had resternotomy for bleeding were excluded (this was planned in the protocol), significantly fewer units of allogeneic blood were transfused in the trial group (65 versus 100 units, relative rate 0.71 p=0.04, see table 2).

Conclusion:
In patients undergoing routine first-time cardiac surgery in an institution with a rigorous blood conservation programme, the addition of cell salvage does not further reduce the proportion of patients exposed to allogeneic blood transfusion. However, patients who do not bleed excessively receive significantly fewer units of blood. This may reduce demand for blood from the national pool. Economic equipoise will be reached if the cost of a unit of blood were to double.

Table 1 Baseline and operative characteristics

Characteristic	Control (n=111)	Cell Saver (n=102)	p
Mean (SD) age	67.4 (10.2)	68.6 (9.6)	0.40
Number (%) male	84 (76%)	78 (76%)	0.98
Median (IQR) logistic EuroSCORE	3.1 (3.6)	3.3 (3.5)	0.67
Median (IQR) days since last aspirin*	7.0 (1.0)	7.0 (1.0)	0.39
Surgery type			0.46
CABG	67 (60%)	64 (63%)	
Valve	30 (27%)	21 (21%)	
CABG + Valve	14 (13%)	17 (17%)	
Priority			0.73
Elective	86 (77%)	76 (75%)	
Urgent	25 (23%)	26 (25%)	
Mean (SD) bypass time (mins)	90.3 (31.1)	89.2 (31.7)	0.79
Mean (SD) cross clamp time (mins)	56.2 (21.2)	55.9 (22.2)	0.93
Mean (SD) CPB to CCU time (mins)	76.3 (20.1)	78.9 (28.0)	0.44
Mean (SD) theatre time (mins)	226.2 (59.3)	229.5 (58.8)	0.69
Median (IQR) intubation time (mins)	511 (381)	556 (368)	0.12
Median (IQR) 6 hr blood loss (mls)	175 (125)	172 (162)	0.10
Median (IQR) total blood loss (mls)	375 (238)	400 (321)	0.88
Number (%) returned to theatre for bleeding	2 (2%)	3 (3%)	0.92
Median (IQR) ICU stay (days)	1.0 (0.0)	1.0 (0.0)	0.80
Median (IQR) hospital stay (days)	7.0 (3.0)	7.0 (5.0)	0.98

*Excludes 28 Cell Saver and 34 Control patients never on aspirin

Table 2 Transfusion products given (excluding first operation for 5 patients returned to theatre for bleeding)

	Control (n=109)	Cell Saver (n=99)	P
Number (%) requiring any RBC or FFP or PLT *	35/109 (32%)	30/99 (30%)	0.90
RBC			
Patients requiring RBC	33 (30%)	28 (28%)	0.87
Total units in theatre	25	24	0.85
Total units in first 6 hours	21	11	0.14
Total units > 6 hours	54	30	0.03
Total	100	65	0.04
FFP			
Patients requiring FFP	6 (6%)	7 (7%)	0.86
Total units in theatre	10	8	0.79
Total units in first 6 hours	11	15	0.31
Total units > 6 hours	7	0	0.98
Total	28	23	0.72
PLT			
Patients requiring PLT	4 (4%)	5 (5%)	0.88
Total units in theatre	2	1	0.62
Total units in first 6 hours	3	4	0.62
Total units > 6 hours	8	0	0.97
Total	13	5	0.10

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SCA18

HIGH-DOSE MAGNESIUM THERAPY DOES NOT DECREASE ATRIAL FIBRILLATION AFTER CARDIAC SURGERY

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Introduction: Atrial fibrillation (AF) is a common complication of cardiac surgery with an incidence ranging between 27-40%. Hypomagnesemia has been associated with an increased risk of postoperative AF. While some studies have suggested a beneficial effect of magnesium (Mg) therapy, almost all of these studies are limited by small sample size and relatively low Mg dose. Therefore, utilizing data from a prospective trial assessing the effect of Mg upon cognitive outcomes, we sought to determine if intraoperative high-dose Mg decreases the occurrence of new-onset postoperative AF.

Methods: After IRB approval, consecutive patients ³55 years in age undergoing primary CABG with or without valve surgery were enrolled into this prospective, randomized, double-blind, placebo-controlled trial. Patients were excluded if they had a history of symptomatic cerebrovascular disease, uncontrolled hypertension, alcoholism, psychiatric illness, creatinine >2 mg/dL, <7th grade education, were pregnant, or had a Mini Mental State Examination score <24. Patients were randomized to receive either placebo or Mg immediately after induction of anesthesia as a 50 mg/kg bolus over 20 minutes followed by another 50 mg/kg infusion over 3 hours (total dose 100 mg/kg). Postoperative AF was diagnosed by telemetry, 12-lead ECG, or physical exam. Patients with a history of chronic or acute preoperative AF were excluded. The 2 treatment groups were compared on patient characteristics with chi-square, rank-sum, or t-tests. The effect of Mg was tested with a chi-square test and with logistic regression accounting for risk of AF using a Risk Index for Atrial Fibrillation after Cardiac Surgery; $p<0.05$ was considered significant.

Results: 168 Mg and 163 placebo patients were analyzed. Mean age was 68 years and mean bypass time was 139 minutes. 78 patients had valve procedures. As expected from randomization, there were no differences between the Mg and placebo groups with respect to demographic characteristics. Serum Mg levels were significantly higher in the Mg treatment group (Figure). The proportions with new-onset AF were 37.5% in the Mg group (95% C.L. 30-45%) compared to 33.7% in the placebo group (95% C.L. 26-41%). The AF risk index, reported as (median, mean±SD), was similar in the treatment groups (Mg: 15.5, 16.8±11.1, compared to placebo: 14, 16.7±11.6); p=0.79. As expected, the AF risk index was different in patients who did (20.5, 21.2±12.4) and did not (13, 14.4±10) develop postoperative AF. No significant effect of Mg was found in the logistic regression analysis adjusting for AF risk (p=0.5). A study with this sample size would have 80% power to detect a difference of about 16%.

Conclusions: Despite significantly higher Mg levels in the intraoperative and immediate postoperative period, high-dose intraoperative Mg therapy did not decrease the incidence of new-onset AF after cardiac surgery.

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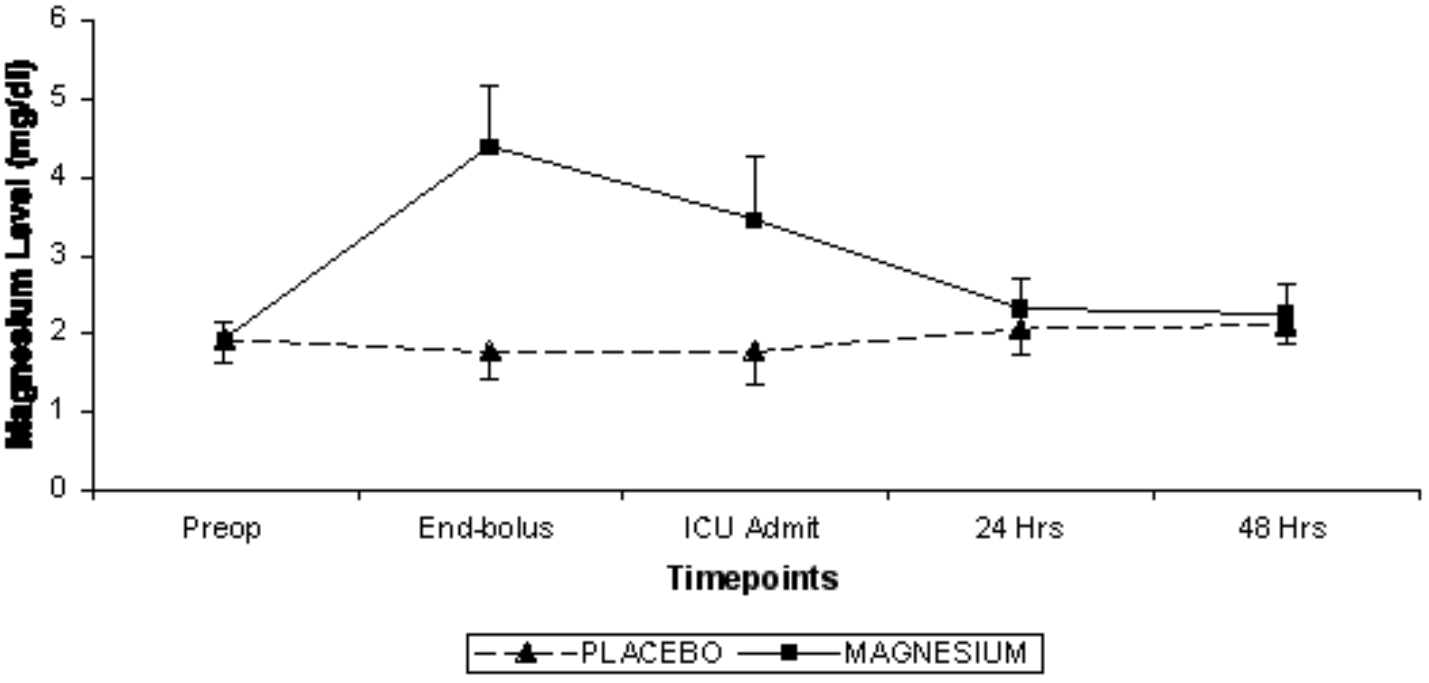

SCA19

DIASTOLIC DYSFUNCTION IS PREDICTIVE OF ADVERSE OUTCOMES FOLLOWING CARDIAC SURGERY INDEPENDENT OF SYSTOLIC FUNCTION

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Introduction: Diastolic dysfunction (DD) has gained attention with the widespread use of perioperative echocardiography for cardiac surgery. DD, defined by conventional Doppler, has been shown to be a predictor of difficulty weaning from cardiopulmonary bypass and greater need for inotropic support independent of systolic function.[1] The effect of DD on other adverse events following cardiac surgery has not yet been investigated, nor have the tissue Doppler, load-independent indices of diastolic function, e´; (mitral annular descent) and E/e´; (filling pressure) been studied in this context.

Accordingly, we hypothesize that e´; and E/e´; will be independent predictors of increased ICU length of stay, total hospital length of stay, need for inotropic support, and total hours requiring mechanical ventilation following cardiac surgery.

Methods: After IRB approval, we retrospectively reviewed echocardiographic data from 205 consecutive patients who underwent cardiac surgery at Wake Forest University under the care of two anesthesiologists. Included were patients having CABG, valve, and CABG with valve surgery. Correlation analyses and hierarchical regression modeling were performed to examine the relationship between e´; E/e´;, and the primary postoperative outcome variables of increased ICU length of stay, total

hospital length of stay, need for inotropic support, and total hours requiring mechanical ventilation following cardiac surgery.

Results: An independent, consistent, and moderate relationship exists between e´;, E/e´; and increased ICU length of stay, total hospital length of stay, need for inotropic support, and total hours requiring mechanical ventilation ($p<0.001$, Table 1). When controlling for comorbidities and ejection fraction, E/e´; is uniquely related to hospital length of stay; an increase in 1 standard deviation of E/e´; value (from a mean of 11 to 17) resulted in an 12% increase in hospital length of stay ($p=0.013$).

Conclusion: These data demonstrate that newer parameters of DD are related to increased hospital length of stay, total ICU hours, need for inotropic support, and total hours requiring mechanical ventilation following cardiac surgery. Furthermore, an elevated E/e´; ratio was predictive of increased post-operative length of hospital stay independent of systolic function. Therefore, tissue Doppler evaluation of diastolic function will aid the clinician in identifying patients at risk for adverse outcomes following cardiac surgery.

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Table 1.

Predictor	LOS: Surgery-DC	Total ICU Hrs.	Inotrope	Total Vent Hrs
EF	-0.09	-0.07	-0.50***	-0.10
E’	-0.24***	-0.26***	-0.29***	-0.29***
E/E’	0.27***	0.29***	0.28***	0.32***

*** p < .001

Note: All correlations are non-parametric (Spearman correlations), except those with Inotrope which are point biserial correlations.

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SCA20

EARLY POSTOPERATIVE NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN (NGAL) PREDICTS ACUTE KIDNEY INJURY (AKI) FOLLOWING CARDIAC SURGERY

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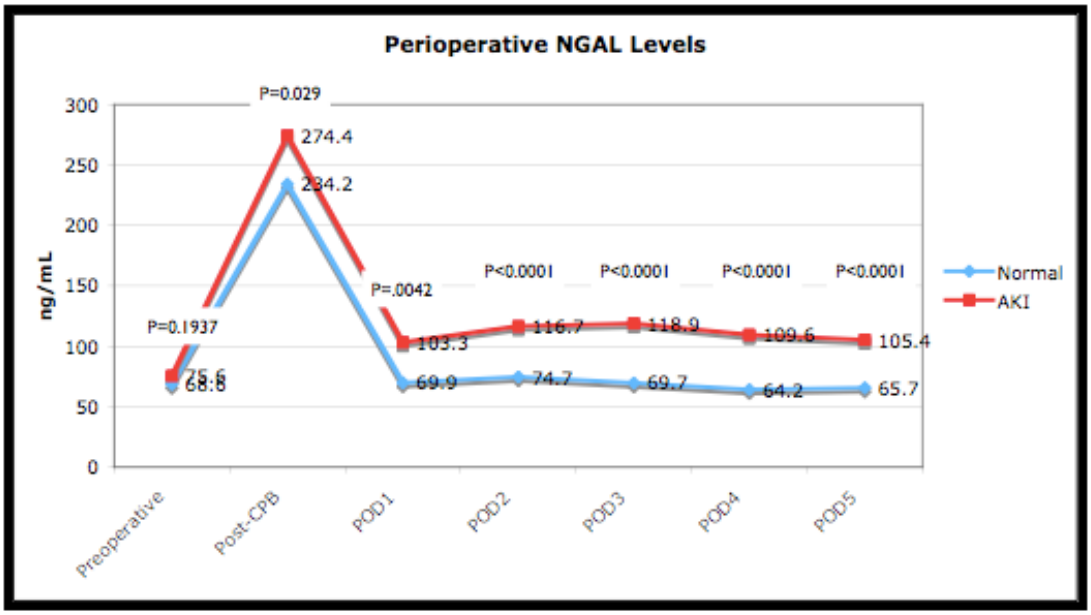
Background: Postoperative AKI is associated with significant postoperative morbidity and mortality. Recognition of AKI is delayed because serum creatinine rises slowly over the course of several days as a response to renal impairment. NGAL has been postulated to be an early marker of AKI following cardiac surgery. We hypothesize that serum NGAL in the immediate postoperative period predicts AKI in adult patients undergoing cardiac surgery with cardiopulmonary bypass (CPB).

Methods: After institutional review board approval, serum NGAL was measured preoperatively, immediately after CPB (post-CPB) and on postoperative days (POD) 1-5 in 1064 adult subjects undergoing cardiac surgery. Exclusion criteria were history of renal replacement therapy, previous kidney transplantation, preoperative serum creatinine ³1.5mg/dL or intraoperative use of aprotinin. AKI was defined as ³50% increase in serum creatinine level above preoperative baseline. An ROC curve was used to determine an optimal cutoff value for serum NGAL measured post-CPB. A Wilcoxon Test was used to compare serum NGAL levels at all perioperative time points. A prediction model was created using multiple stepwise logistic regression.

Results: After applying exclusion criteria, the incidence of AKI was 8.2% in 915 subjects. Preoperative NGAL levels were 76±44 ng/mL [mean±SD] in subjects who developed postoperative AKI vs. 69±31 ng/mL (P=0.194) when compared with those who did not. In individuals who developed AKI, post-CPB serum NGAL levels were significantly elevated (274±139 ng/mL vs. 234±105 ng/mL; P=0.029), and remained significantly elevated through POD 5 (see Table). After adjusting for age, gender, race, body mass index, CPB time, pre- or intraoperative transfusion of leukocyte-replete packed red blood cells, and pre- and post-CPB serum creatinine, post-CPB serum NGAL, dichotomized at 474ng/mL, remained a statistically significant independent predictor of AKI (OR = 2.28; 95% CI =1.44, 3.53; P=0.0003). The optimal post-CPB serum NGAL cutoff based on the ROC curve had a specificity of 97.2%, but a poor sensitivity of 15.4%.

Conclusion: Elevated serum NGAL levels immediately following CPB are an independent predictor of postoperative AKI in patients undergoing cardiac surgery. While highly specific, its usefulness as an early indicator of postoperative AKI is limited by poor sensitivity.



SCA21

THE EFFECT OF SINGLE DOSE INTRAVENOUS AMIODARONE IN PATIENTS WITH RHEUMATIC ATRIAL FIBRILLATION UNDERGOING VALVULAR HEART SURGERY

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Background: Atrial fibrillation (AF) is associated with the risk of thromboembolic complications. Maintenance of normal sinus rhythm (NSR) is superior to ventricular rate control in patients with rheumatic AF (1). We evaluated the utility of a single dose of intravenous amiodarone given intraoperativly in converting the rheumatic AF into NSR, in patients undergoing valvular heart surgery.

Materials & methods: Eighty two patients with rheumatic valvular heart disease, who have persistent AF, were randomly assigned in a double blind fashion to either an amiodarone group (42) or control group (40). The amiodarone group received injection amiodarone 3mg/kg in 100 ml of normal saline, while in control group same volume of normal saline was given. The infusion was started before skin incision & given over the period of 30 minutes. The anesthetic, cardio pulmonary bypass and surgical techniques were standardized in both groups. First rhythm after the release of aortic cross clamp was noted. If the patient had AF, synchronized cardioversion was attempted. If heart rate was less than 60 beats per minute, atrial pacing was initiated. The recurrence of AF at the end of surgical procedure and in the first 24 hour of post operative period, the need and energy required for cardioversion, duration of intensive care unit (ICU) stay was noted.

Results: The primary outcomes of the study are displayed in table. In both the groups the mean pre operative left atrial (LA) size of patients with AF on the first post operative day (amiodarone group- 56.11± 10.96 mm, control group- 50.82 ± 9.29mm) was significantly greater than those without AF (amiodarone group- 47.24± 10.76 mm, control group- 44.5± 6.62 mm) (p = 0.035). In amiodarone group, 7 out of 9 patients those developed AF (at first post operative day), had LA size ³ 60 mm.

Conclusion: An intra operative single dose (3 mg/kg) of intravenous amiodarone increased the conversion rate of AF to NSR, reduced the need & energy required for cardioversion (2), reduced the recurrence of AF within one day and reduced the ventricular rate in those not converted to NSR. It also reduced the duration of ICU stay. However a larger preoperative LA size may be associated with higher recurrence rate of AF despite treatment with single dose amiodarone (3).

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Primary outcomes	Amiodarone group (n = 42)	Control group (n = 40)	p value
First rhythm at Aortic clamp release- No of patients			0.035*
AF	6 (14.3%)	15 (37.5%)	
Normal Sinus Rhythm	31 (73.8%)	17 (42.5%)	
Junctional Rhythm	2 (4.8%)	3 (7.5%)	
Ventricular.Tachycardia/ Fibrillation	3 (7.1%)	5 (12.5%)	
No of patients responding to cardioversion/defibrillation	6/8 (75%)	9/19 (47.4%)	0.187
No of cardioversion/defibrillation needed per patient	1.5±0.54[f]	2.26±0.73[f]	0.014*
Amount of energy needed- joules	22.5±8.86[f]	40.53±16.5[f]	0.008*
AF at end of surgery-No of patients	4 (9.5%)	13 (32.5%)	0.01*
Recurrence of AF in ICU- No of patients	5/ 39 (12.8)	9/27 (33.3%)	0.045*
Need for temporary pacing- No of patients	17 (40.5%)	8 (20%)	0.04*
No of patients with AF at 1 st postoperative day	9 (21.4%)	22 (55%)	0.002*
Ventricular rate in patients with AF at first post operative day- bpm	72.89±11.27[f]	92±15.3[f]	0.002*
ICU stay- hours	41.67 ±4.97[f]	47.33 ±7.09[f]	< 0.001*

* P < 0.05 is statistically significant [f]mean± standard deviation

AF – atrial fibrillation ICU – intensive care unit bpm – beats per minute

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SCA22

AN INVESTIGATION OF THE COMPARATIVE VALIDITY OF BNP AND TROPONIN-I FOR MEASUREMENT OF ISCHEMIA-REPERFUSION INJURY IN HEART TRANSPLANTATION

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Introduction

Troponin is used as a bio-marker for the measurement of ischemia-reperfusion (I-R) injury in heart transplantation but may not be the most appropriate marker available. While troponin is released from dying myocytes a component of I-R injury is due to sub-lethal injury to myocytes that ultimately recover. Brain Natriuretic Peptide (BNP) is released from cardiac myocytes in response to stretch, inflammation and ischemia. It does not require myocyte death for release and may offer greater specificity than troponin in the measurement of I-R injury. However, it has not been validated for this purpose in cardiac transplantation. Sensitive, specific and valid biomarkers are essential for use in clinical trials testing interventions to reduce acute allograft I-R injury. We hypothesized that BNP is a valid marker of cardiac I-R injury.

Methods

We performed a prospective observational study in 25 patients undergoing heart transplantation. We recorded donor BNP and troponin-I levels at the time of procurement and recipient BNP and troponin-I levels pre-operatively, at allograft reperfusion and at Day 1, 2, 3 and 7 postoperatively. We hypothesized that a valid biomarker would correlate with other parameters believed to worsen the I-R injury. We further hypothesized that a valid biomarker would correlate with early postoperative markers of impaired cardiac function. Summary measures of both BNP and troponin-I were assessed for correlation with parameters likely to contribute to a more severe I-R injury and also with outcomes indicative of a more severe I-R injury, including inotropic support and mechanical circulatory support. We further assessed correlation between BNP and troponin-I.

Results

Day-1 BNP correlated with allograft ischemic time (r=0.44, 95% C.I. 0.05-0.71, p=0.03), donor BNP (r=0.64, 95% C.I. 0.30-0.84, p=0.001) and donor troponin-I (r=0.57, 95% C.I. 0.23-0.80, p=0.003). There was no correlation between Day-1 troponin-I and allograft ischemic time (r=0.03, 95% C.I. -0.36 to 0.43, p=0.86), donor BNP (r=0.04, 95% C.I. -0.39 to 0.46, p=0.85) or donor troponin-I (r=0.07, 95% C.I. -0.35 to 0.46, p=0.75).

Day-1 BNP had the strongest correlation of either marker (r=0.27, p=0.19) with inotropic support. However, when stratified by ECMO status, BNP better correlated with inotropic support in patients requiring ECMO (r=0.70, 95% C.I. 0.13-0.92, p=0.02), while troponin-I correlated better with levels of inotropic support (r=0.52, 95% C.I. 0.01-0.81, p=0.049) in patients not requiring ECMO. Patients requiring mechanical circulatory support in the early postoperative period had higher levels of both BNP and troponin-I. Postoperative levels of BNP and troponin-I correlated poorly with each other (r=0.19, 95% C.I. -0.22 to 0.55, p=0.45).

Conclusion

We have demonstrated construct validity for BNP as a quantitative measure of I-R injury in heart transplantation. BNP correlates better with various parameters of injury severity than does troponin-I. The poor correlation between postoperative BNP and troponin suggest they are measuring different aspects of myocardial injury. This may explain the difference in biomarker correlation with postoperative inotropic support when stratified by ECMO status.

SCA23

IDENTIFICATION OF COMMON GENETIC VARIANTS ASSOCIATED WITH SEVERE POSTOPERATIVE BLEEDING AFTER CORONARY ARTERY BYPASS GRAFT SURGERY

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Background

Postoperative bleeding after cardiac surgery, requiring coagulation factor transfusion or reoperation, is associated with longer hospital stays and increased 1-year mortality. Circulating levels of coagulation proteins have been shown to be highly heritable in the ambulatory population. Therefore, we hypothesized that variation in the genes of the coagulation, fibrinolytic, and platelet and cell ligand receptor pathways are associated with bleeding outcomes after coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass (CPB).

Methods

This multi-institutional study examined the association between postoperative bleeding, defined as chest tube drainage > 750 mL in the first eight hours postoperatively, and genes coding for 27 proteins of platelet receptors (protease activated receptors 1,3 and 4, glycoproteins Ia, Iba, Ibb, IIb, IIIa, V, VI and IX), coagulation (factors II, III, V, VII; X, fibrinogen a, b and γ;, and tissue factor), anticoagulation (antithrombin, protein C, thrombomodulin, and tissue factor pathway inhibitor), anti-fibrinolysis (plasminogen activator inhibitor-1 and thrombin activatable fibrinolysis inhibitor) and a cell-cell adhesion ligand (P-selectin). Genes were chosen a priori based on their role in regulating hemostasis.

Single nucleotide polymorphisms (SNPs) were considered to be associated with bleeding if they met three testing criteria: single SNP association, single SNP logistic regression, and set association. To determine whether these candidate SNPs accounted for the risk of severe bleeding beyond the extent explained by clinical variables, unconditional binominal logistic regression was used to assess the marker association, while adjusting for previously-identified clinical covariates.

Results

Of the 1167 patients enrolled into the source cohort during the study period, 347 were excluded from analysis for one or more of the following exclusion criteria: non-Caucasian race, emergency surgery, prior cardiac surgery, CPB not used, unplanned concurrent valve surgery performed, missing genotype data. After adjustment for institution, lower BMI, ε;-aminocaproic acid use and the absence of diabetes were significant independent predictors of severe postoperative bleeding. Other demographic and previously identified predictors of bleeding were also included in the clinical model in order to maximize its predictive value.

After exclusion of 106 SNPs for quality control, 467 SNPs remained which were examined using trend, dominant, and recessive models and accounted for multiple comparisons by permuting case:control status. Fifteen SNPs from nine genes (CPB2, F2, F2R, F2RL2, F5, FGA, ITGA2B, TFPI, THBD) fulfilled the criteria for association with bleeding after adjustment for clinical covariates (Table 1).

Conclusion

We found an association between 15 SNPs in nine candidate genes with postoperative chest tube drainage after CABG surgery.

Table 1: Final common set of candiate SNPs from single SNP association or single SNP logistic regression; empirical (permuted) P-value <0.05, while accounting for clinical covariates.

SNP	Position	Alleles	Gene	model	OR	95% CI	P value for	Role	Amino acid change	Amino acid position
rs3742266	Chr13:45577040	G/A	CPB2	Dominant	0.488	0.235-1.013	0.048	Intron-exon boundary		
rs3136456	Chr11:46702437	C/A	F2	Dominant	1.92	0.971-3.799	0.045	Intron		
rs250737	Chr5:76069058	A/T	F2R	Additive	1.5	0.989-2.275	0.046	Downstream		
rs250751	Chr5:76074641	G/A	F2R	Additive	0.567	0.372-0.864	0.006	Downstream		
rs2069656	Chr5:75953389	C/T	F2RL2	Additive	0.583	0.356-0.954	0.026	Intron		
rs17567779	Chr5:75961672	G/A	F2RL2	Additive	0.271	0.080-0.924	0.029	Promoter		
rs4525	Chr1:167778358	A/G	F5	Dominant	1.736	0.997-3.024	0.046	Coding exon	H/R	865
rs2070027	Chr4:155729831	T/C	FGA	Additive	2.164	0.912-5.138	0.046	Intron		
rs9890900	Chr17:39815623	T/C	ITGA2B	Additive	0.156	0.035-0.701	0.004	Intron		
rs2192824	Chr2:188077036	C/T	TFPI	Recessive	0.394	0.159-0.973	0.037	Intron		
rs2192825	Chr2:188099064	T/C	TFPI	Recessive	0.376	0.150-0.942	0.037	Intron		
rs7594359	Chr2:188117093	C/T	TFPI	Recessive	0.392	0.176-0.875	0.018	Intron		
rs10203579	Chr2:188132664	G/T	TFPI	Recessive	0.44	0.233-0.833	0.01	Promoter		
rs4667169	Chr2:188135499	T/C	TFPI	Recessive	0.371	0.176-0.781	0.01	Promoter		
rs6076016	Chr20:22982597	T/A	THBD	Additive	1.469	1.018-2.121	0.033	Promoter		

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SCA24

HEART-TYPE FATTY ACID BINDING PROTEIN IS AN EARLY-PEAKING AND INDEPENDENT PREDICTOR OF DEATH AFTER CORONARY ARTERY BYPASS GRAFT SURGERY

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Background: Heart-type fatty acid binding protein (hFABP) is a small cytosolic protein abundantly present in the myocardium and is the key cytosolic transporter of fatty acids. Previous studies in the ambulatory setting have associated hFABP with an increased risk of death and major cardiac events. Its prognostic utility in the cardiac surgical population has not been established.

Methods: As part of a prospective, multi-institutional study, we measured hFABP, cardiac Troponin I (cTnI), and the MB fraction of creatine kinase (CKMB) in 1442 patients undergoing coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB) at seven time points (preoperative, post-CPB and postoperatively on days 1-5). Patients were followed for up to 5 years (mean 3.3 ±1.4 yrs). Multivariable linear regression analyses of hospital length of stay (HLOS) were performed, adjusting for preoperative baseline variables including age, gender, institution, and intraoperative clinical characteristics. We estimated the independent prognostic utility of hFABP on long-term survival using a Cox proportional-hazard model associated with elevated levels of the three biomarkers, while adjusting for preoperative baseline variables.

Results: hFABP levels were markedly elevated after CABG surgery, peaking immediately after termination of CPB. By contrast, cTnI and CKMB peaked on the first postoperative day (Figure 1). Multivariate model fit for HLOS was significantly improved by separate inclusion of each of the biomarkers to the clinical model: (clinical model r2= 0.111), peak CKMB & clinical model (r2=0.117; P<0.01), peak cTnI & clinical model (r2=0.122; P<0.01), peak hFABP & clinical model (r2=0.123; P<0.01).

Multivariable Cox proportional hazards model for survival only showed significant improvement with the addition of hFABP: (clinical model r2= 0.064), peak CKMB & clinical model (r2=0.065; P=0.14), peak cTnI & clinical model (r2=0.065; P=0.30), peak hFABP & clinical model (r2=0.075; P<0.0001).

Conclusion: hFABP peaks earlier after primary CABG surgery than traditional biomarkers of myocardial injury. Peak postoperative hFABP is a better predictor of death than other commonly used biomarkers. This effect is independent of other established clinical risk predictors. hFABP may offer advantages in quantifying intermediate and long-term effects of myocardial injury following CABG surgery.

Figure 1: Median time course of Biomarkers (± standard error)