unstable if they were still receiving any vasoactive drug (vasopressin, epinephrine, norepinephrine, or dopamine).

RESULTS: Mean age was 65 ± 10 years and 72% of patients were male. Surgical procedures included coronary artery bypass grafting in 55 (41%) patients, valvular surgery in 41 (30%), replacement of the ascending thoracic aorta in 9 (7%) and a combined procedure in 25 (19%). Fifty-six percent of patients showed postoperative relative adrenal insufficiency. Compared to patients who showed a normal response to the cosyntropin stimulation test, patients who presented relative adrenal insufficiency had significantly higher rates of hemodynamic instability at 48 hours (40% vs 22%, p=0.026) and a longer duration of intensive care unit stay (8.0 ± 17.9 vs 2.6 ± 4.5 days, p=0.02). In-hospital mortality occurred in 6 (9%) patients from the relative adrenal insufficiency group and 1 patient (2%) from the control group (p = 0.12). Upon multivariate analysis, adrenal response to the cosyntropin test was a significant independent predictor of hemodynamic instability at 48 hours after surgery (OR 0.94 [0.90 - 0.98] per 10 nmol/L cortisol increase; p=0.001). Other risk factors for hemodynamic instability at 48 hours postoperatively are presented in Table 1. Among perioperative survivors, survival at 1, 5 and 10 years was 94 ± 3%, 81 ± 5%, 69 ± 6% versus 96 ± 3%, 91 ± 4%, 81 ± 5% in the relative adrenal insufficiency and control groups, respectively (p=0.11). Long-term survival in each group is depicted in Figure 1.

CONCLUSION: Postoperative relative adrenal insufficiency is common in patients undergoing heart surgery and is associated with an increased risk of persistent hemodynamic instability and prolonged intensive care unit stay.

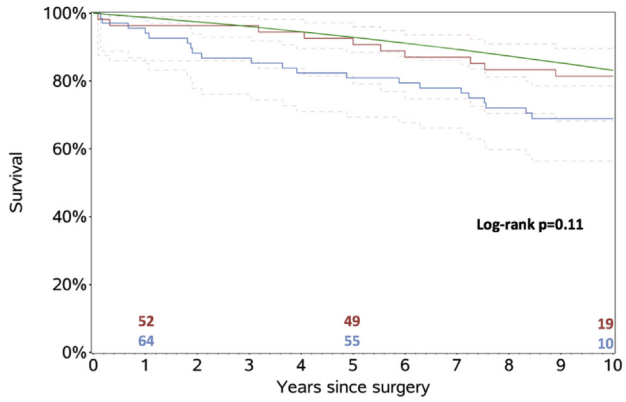
Table 1. Multivariate results for factors associated with hemodynamic instability at 48 hours after surgery

Risk factors	OR (95% CI)	*p-value*
Cortisol increase (per 10 nmol/L) †	0.94 (0.90-0.98)	0.002
Age (per 10 years)	1.86 (1.12-3.09)	0.016
Female sex	3.22 (1.20-8.63)	0.020
Preoperative LVEF (per 10%)	0.34 (0.21-0.55)	<0.001

**Definition of abbreviations*: CI = confidence interval; LVEF = left ventricular ejection fraction; OR = odds ratio.

† Peak cortisol increase following ACTH stimulation test 36 hours after surgery.

Figure 1: Survival of patients with (blue) and without (red) postoperative adrenal insufficiency compared to the age- and gender-matched general population (green) (*excluding operative deaths*)



063
FLUOROQUINOLONE INDUCES HUMAN AORTIC FIBROBLAST-MEDIATED EXTRACELLULAR MATRIX DYSREGULATION

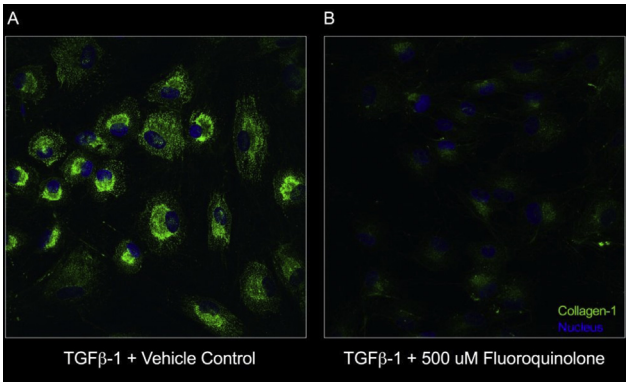
D Guzzardi, G Teng, D Svystonyuk, S Kang, D Park, D Belke, J Turnbull, P Fedak

Calgary, Alberta

BACKGROUND: Use of fluoroquinolone (FQ) antibiotics is common and widespread in the community. FQ are highly associated with connective tissue weakening causing severe tendon ruptures. Clinical studies have also shown increased aortic events after FQ exposure. It is possible that a similar mechanism of connective tissue weakening may exacerbate aortopathy leading to aortic rupture/dissection after exposure to FQ. Aortic fibroblasts mediate extracellular matrix (ECM) homeostasis and prevent aortic rupture by synthesizing collagen matrix and expressing endogenous protease inhibitors (TIMP). We hypothesized that FQ induces ECM dysregulation by downregulating collagen and TIMP expression thereby increasing the capacity for matrix metalloproteinase (MMP)-mediated ECM disruption.

METHODS AND RESULTS: Human aortic fibroblasts were isolated from patients with aortopathy undergoing elective ascending aortic resection (N=4). Ciprofloxacin at a tissue-relevant concentration of 500uM was used as the representative FQ. We assessed the capacity for ECM degradation by comparing MMP and TIMP protein expression using multiplex in human aortic fibroblasts exposed to FQ for 48 hours versus 0.8uM hydrochloric acid vehicle control. FQ significantly decreased TIMP-1 (0.21 ± 0.08 vs 0.95 ± 0.24pg/mL, p=0.03) and TIMP-2 (0.27 ± 0.06 vs 1.12 ± 0.22pg/mL, p=0.01) concentrations. MMP-1, -3, -10 and -13 were unaffected by FQ. These data confirm an increased capacity for MMP-mediated ECM degradation. Aortic fibroblasts were stimulated with transforming growth factor -1 and incubated with FQ. Western blotting of cell lysate revealed decreased collagen-1 expression at 500uM FQ versus vehicle control (0.02 ± 0.01 vs 0.70 ± 0.08 optical density relative to GAPDH, p=0.01). Congruent with these findings, immunofluorescent staining of aortic fibroblasts showed decreased intracellular collagen-1 with FQ as compared to vehicle control (Figure 1B vs 1A). We assessed apoptosis and necrosis via annexin V and propidium iodide staining, respectively. Low and non-significantly different apoptosis/necrosis compared to vehicle control was observed (1.83 ± 1.09 vs 1.40 ± 0.40% apoptotic/necrotic cells, p=0.73). These data confirm that the observed effects were not the result of increased cell death from FQ exposure.

CONCLUSION: For the first time, we document that human aortic fibroblasts exposed to FQ show an increased capacity for ECM dysregulation by reduced collagen and TIMP protein expression. These data may provide a novel mechanism to explain the increased clinical incidence of aortic events for patients exposed to FQ. FQ may exacerbate aortopathy and these data suggest caution for use of FQ in such patients.



Alberta Innovates Health Solutions (AIHS)

064
SINGLE CENTRE EXPERIENCE WITH LONG-TERM FOLLOW-UP OF RECOMBINANT FACTOR VIIA IN PATIENTS UNDERGOING CARDIAC SURGERY

Z Engelbrecht, S Connors, M Valdis, N Hache, C Yegappan, K Melvin, G Zbitnew, S Tierney, C Adams

St. John's, Newfoundland and Labrador

BACKGROUND: Peri-operative haemorrhage requiring massive transfusion represents a major challenge in cardiac surgery and is associated with significant morbidity and mortality. Recombinant Factor VIIa (rFVIIa) administration remains a controversial rescue therapy for intractable non-surgical bleeding. Variability in reported complications by small retrospective studies has led to a disparity in recommendations found in the literature.

METHODS AND RESULTS: We report a single centre experience of 103 consecutive patients who received rFVIIa for intractable non-surgical haemorrhage after cardiac surgery from 2010 to 2014. Retrospective data analysis was performed. The primary end point was a combined incidence of major adverse thromboembolic events (MATEs), which included CVAs, post-operative MI, acute mesenteric ischemia, and significant peripheral arterial ischemia. Secondary end points included chest tube loss and blood product utilization 24 hours pre- and post-rFVIIa administration, and 30-day mortality. All reported CVAs were reviewed by a single neuroradiologist to confirm diagnosis, location, and extent. A total of 103 consecutive cardiac surgery patients received rFVIIa for intractable non-surgical bleeding: 10 isolated AVR, 27 isolated CABG, 31 combined CABG/valve, 14 Bentall/Root procedure, 5 Type A aortic dissection and 16 other categorized. A median dose of 6.7mg of rFVIIa was administered (Range 2.4 to 14.8mg). rFVIIa administration occurred both in the OR (46.6%) and in the ICU (53.4%). The median age was 66 yrs (±11.9) with 71% being male. The overall incidence of MATEs was 14.6% and was comprised of 8.7% CVA, 2.9% MI, and 2.9% ischemic gut. There were no acute peripheral arterial vascular events requiring intervention. Chest tube drainage before and after rFVIIa decreased from 1300ml/hr to 376.5ml/hr ($p < 0.001$). Blood product utilization was significantly decreased in the 24 hours after rFVIIa administration ($p < 0.001$): PRBCs 5.1 to 2.7 units; platelets 1.3 to 0.5 units; FFP 6.2 to 2.2 units. The rate of re-exploration due to bleeding was 42%. Overall 30-day mortality was 21%. A survival curve was created for a subset of patients (N=66) who had surgery between 2010 and 2013. In this subset the mortality rate was 24.2% with a mean survival time of 12.5 months (Range 0-46).

CONCLUSION: This large case series of Canadian cardiac surgery patients with intractable life-threatening bleeding demonstrates that administration of rFVIIa is an effective rescue therapy with an acceptable rate of MATEs, given the likely alternative outcomes, in salvage situations when conventional therapies have failed.

Table 1. Clinical Outcomes of Cardiac Surgery Patients Following rFVIIa Administration for Bleeding

Outcome	Value[1]	*P* value[2]
Total MATEs	15 (14.6%)	-
CVA[3]	9 (8.7%)	-
MI	3 (2.9%)	-
PAI	0 (0%)	-
Ischemic gut	3 (2.9%)	-
30-day Mortality	22 (21.4%)	-
Chest Tube Drainage (ml/hr)		
Pre	1300.3 ± 988.2	
Post	376.5 ± 2250.5	<0.001
PRBCs transfused (units)		
Pre	5.1 ± 3.1	
Post	2.7 ± 2.6	<0.001
Platelets transfused (units)		
Pre	1.3 ± 0.7	
Post	0.5 ± 0.8	<0.001
FFP transfused (units)		
Pre	6.2 ± 2.9	
Post	2.2 ± 3.4	<0.001

MATEs major adverse thromboembolic events, *CVA* cerebral vascular accident *AVR* aortic valve replacement, *MI* myocardial infraction, *PAI* peripheral arterial ischemia, *PRBCs* packed red blood cells, *FFP* fresh frozen plasma
Values are presented as n (%) or mean ± SD where appropriate
[1] Total patients N=103
[2] *P* values relate to paired T-tests of values 24-hr before and after rFVIIa administration
[3] Reported CVAs were further reviewed by a neuroradiologist and only patients whose diagnosis was confirmed were included

Canadian Pediatric Cardiology Association (CPCA) Moderated Presentations
2017 CCS RESEARCH HIGHLIGHTS IN CONGENITAL HEART DISEASE
Saturday, October 21, 2017

067
IMPACT OF FENESTRATION ON POSTOPERATIVE COMPLICATIONS FOLLOWING A FONTAN PROCEDURE: SYSTEMATIC REVIEW AND META-ANALYSIS

I Bouhout, W Ben-ali, P Khairy, N Poirier

Montréal, Québec

BACKGROUND: A systematic review and meta-analysis of studies were performed comparing fenestrated and non-fenestrated Fontan procedures.

METHODS: Medline and Embase were searched with the following strategy: ([Fenestration OR Fenestrated] AND [Fontan OR cavopulmonary connection) from 1990 to 2017.