

### SCA 3

#### THE EFFECT OF HIGH DOSE RECOMBINANT FACTOR VIIA ON VASCULAR GRAFT PATENCY

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**Introduction:** Despite major improvements in care of patients undergoing cardiac surgery, excessive bleeding remains a significant problem. Recently, some reports have described the use of recombinant factor VIIa (rVIIa) to decrease bleeding in cardiac surgery(1;2). These case reports suggest recombinant factor VIIa may be an alternative when other management options have been exhausted. However, the potential hemostatic benefits of rVIIa could be negated if, in combination with tissue factor expression and thrombin generation at the site of new anastomoses, it resulted in graft occlusion(3). The objective of this safety study was to determine if the administration of 300ug/kg rVIIa reduces graft patency at the site of new vascular anastomosis in a rabbit model.

**Methods:** After Animal Care Committee approval, 11 rabbits were anesthetized with ketamine (10mg/kg), xylazine (2mg/kg) and isoflurane (1-2% in oxygen). An arterial cannula was inserted into an ear artery for blood sampling and monitoring of blood pressure. Through a midline neck incision, both carotid arteries and the right jugular vein were isolated. The animals were then anticoagulated with heparin (300 IU/kg) to maintain an activated clotting time (ACT) of greater than 300 seconds. A 2-3 cm portion of the jugular vein was excised, and a reversed venous graft with end to side anastomoses on the ligated right carotid artery was fashioned using 9-0 prolene sutures. The left carotid artery was then transected and reanastomosed in an end to end manner. After the completion

of the last graft, protamine (3-5 mg/kg) was administered. Graft patency was ensured prior to skin closure. Animals were then given either rVIIa (300 ug/kg IV) or placebo. The primary outcome was graft patency, measured 3 and 24 hours postoperatively using vascular ultrasound and/or direct inspection. Rabbits were sacrificed if there was evidence of thrombus (or no flow) at the early ultrasound, or at 24 hours. At sacrifice, macroscopic evidence of thrombus was assessed. Data was analyzed using chi-square, fisher's exact test, or ANOVA where appropriate, with  $p < 0.05$  considered significant.

**Results:** 5 animals received rVIIa and 5 received placebo. One animal was excluded because of graft occlusion prior to drug administration. All of the factor rVIIa treated rabbits demonstrated either ultrasound evidence of graft non-patency or macroscopic evidence of occlusive thrombus at sacrifice, whereas all of the control animals had evidence of flow through the grafts ( $p < 0.001$ ). One of the control animals who demonstrated initial graft patency on ultrasound died unexpectedly before the 24 hour assessment. There were no significant differences in PaO<sub>2</sub> or ACT levels between groups.

**Discussion:** The preliminary results from this animal study suggest that high doses of rVIIa (300 ug/kg) are associated with an increased incidence of occlusion of new vascular grafts. Whether such effects occur at lower doses, remains to be determined. This study may help to guide the clinical use of rVIIa after cardiac and vascular surgery.

#### References

- (1) Can J Anaesth 2003; 50(6):599.
- (2) Anesth Analg 2001; 93(2):287.
- (3) Anesth Analg 2002; 94(5):1369.