The use of recombinant Factor VIIa has become a necessary part of the clinician’s armamentarium for treatment of excessive bleeding after cardiac surgery. Excessive blood loss occurs in 4-32% of patients undergoing cardiac surgery. The potential causes of this excessive bleeding include activation of the coagulation cascade, fibrinolysis, surgical trauma, enhanced thrombin generation from cardiopulmonary bypass, hemodilution of clotting factors and drugs that impair platelet function. Often, more than one of these potential etiologic factors will act in concert to cause excessive hemorrhage. Surgical exploration is often required. Adverse outcomes in cardiac surgery are associated with both surgical reexploration and excessive bleeding. The development of new therapies that either prevent excessive bleeding or control hemorrhage are necessary and important therapeutic tools. Bleeding after cardiac surgery is either due to surgical factors or the development of coagulopathy. Regardless of the cause, transfusion of blood and blood products is also associated with significant adverse effects. Transfusion of red blood cells (RBC) has been shown to be associated with immune modulation resulting in increased risk of infection perioperatively, development of multiple organ failure, adult respiratory distress syndrome (ARDS) and transfusion related acute lung injury (TRALI). The transfusion of platelets, cryoprecipitate and fresh frozen plasma is associated with higher risk of bacterial contamination (platelets) and TRALI (all components) compared to RBC transfusion. Therefore therapies to reduce the amount of transfusion when excessive bleeding occurs are highly desirable to potentially limit morbidity and mortality. Recombinant activated factor VII (rFVIIa) has been used to treat hemorrhage after cardiac surgery. The use of rFVIIa for the treatment of hemorrhage following trauma or major surgical procedures is off-label and considered rescue therapy. The first reported off label use of rFVIIa for massive hemorrhage was in 1999 with a case report of clinical efficacy in a pt with life-threatening hemorrhage from a GSW to the abdomen. Since that time there has been a plethora of reports touting its clinical efficacy in stemming massive hemorrhage. The initial support for the use of rFVIIa in excessively bleeding patients post-cardiac surgery was based largely on published anecdotal case reports and small case series. There are no randomised, placebo-controlled, double blind trials, which have reported a substantial reduction in bleeding with the use of rFVIIa. Recently however, there have been a number of observational studies which
have shown a reduction in excessive bleeding after use of rFVIIa in post-cardiotomy patients.\textsuperscript{x,xi,xii,xiii}

The largest of these observational studies was reported in Circulation in 2008.\textsuperscript{10} This report described the use of Factor VII in Canada at 18 heart surgery centers from 2003 to 2006. 522 patients received rFVIIa during this time period and data were collected on 502 of this cohort. This group found that following the administration of rFVIIa there was a reduction in the amount of RBC units transfused. Prior to administration the median transfusion was 8 units of RBC, and just 2 units following. There were a number of other clinically significant findings of this review. These reviewers looked at the patients who did not respond to rFVIIa administration. A recent report from the New Zealand and Australian Haemostasis register has suggested that the presence of acidosis adversely affected the efficacy of response to rFVIIa.\textsuperscript{xiv} In the Canadian review the only independent variables associated with lack of response to rFVIIa were the presence of abnormal coagulation parameters and the transfusion of >15 units of RBC prior to administration of rFVIIa.\textsuperscript{10} The “early” use of rFVIIa i.e. prior to the transfusion of 8 units of RBC’s has been previously shown to be beneficial.\textsuperscript{12}

Despite the multiple publications over the past 5 years touting the effectiveness of rFVIIa, there still remain troubling concerns about its safety with widespread use. Some of the concern stems from the proposed mechanism of action of rFVIIa, which involves binding to tissue factor. The use of cardiopulmonary bypass during cardiac surgery is associated with activation of tissue factor.\textsuperscript{xv} It has been theorized that rFVIIa may bind to circulating activated tissue factor resulting in widespread thrombosis. There are multiple case reports in the literature describing adverse thromboembolic events in association with the administration of rFVIIa.\textsuperscript{xvi,xvii,xviii} Despite case reports and anecdotal information it is still unknown whether this hemostatic agent is safe. Some of the adverse events reported included myocardial infarctions, stroke and thrombosis. Risk-adjusted analysis of adverse event rates in patients treated with rFVIIa for excessive bleeding after cardiac surgery have not shown an increased event rate in treated patients when compared to a cohort with identical bleeding rates and transfusion.\textsuperscript{12} Most investigators agree that without a randomised controlled clinical trial the safety of rFVIIa use will be unknown.
References


