

remained unchanged (Table 2). In 16 cases bleeding stopped 10–30 min following the injection, and decreased dramatically in six cases. Six patients did not achieve effective hemostasis after administration of rFVIIa. Bleeding reoccurred in seven cases after 6 hours and more following infusion of rFVIIa. In 25 cases no adverse events were reported; two patients developed high temperature (38.7°C and 39.0°C) within 15 min after the injection of rFVIIa. The described observations suggest efficiency of rFVIIa in controlling the postoperative and spontaneous bleeding in patients with various types of thrombocytopenia. Nevertheless, the laboratory tests do not always correlate with clinical efficiency of this treatment.

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Use of recombinant activated factor VII after paediatric cardiac surgery

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Objective To evaluate the opportunities of recombinant activated factor VII (rFVIIa) in pediatric patients with bleeding after cardiac surgery.

Methods Since January 2003, 90 pediatric patients received rFVIIa for bleeding after cardiac surgery. Indications for rFVIIa were the following: prevention of bleeding after major surgery in newborns (arterial switch operation, radical correction of truncus arteriosus, Norwood's procedure) or bleeding rate 5 ml/kg/hour and more in older children – 75 patients (group A); severe tracheal bleeding in sepsis and multiple organ failure – six patients (group B); uncontrolled bleeding during total cardiopulmonary bypass with ECMO – nine patients (group C). Children's age was 2 days–18 years, body weight was 1.7–89 kg.

In group A the mean cardiopulmonary bypass time was 223 ± 29 min (108–423 min). Before rFVIIa was used the thrombocyte quantity increased up to $60 \times 10^9/l$, the ACT time was less 180 s and the body temperature was more than 35°C. FVIIa (120 µg/kg) was used 10–45 min after bypass. If needed, a repeated dose of 120 µg/kg was given after 1–1.5 hours (36 patients).

In group B severe tracheal bleeding developed in ventilated patients despite thrombocyte transfusions and 5000 UE/kg/hour aprotinin. rFVIIa was used in all patients twice (120 µg/kg).

In group C severe bleeding (8–42 ml/kg/hour) occurred during cardiopulmonary bypass with ECMO. Before rFVIIa administration the ACT was maintained between 180 and 200 s, the PLT quantity was not below $50 \times 10^9/l$ and the aprotinin infusion rate was 10,000 UE/kg/hour. In all cases rFVIIa was used twice with a dose of 120 µg/kg.

Results In group A bleeding stoppage (<1 ml/kg/hour) was reached in 49 patients (65.3%) 40–75 min after FVIIa administration; in 17 cases (22.7%) the bleeding rate decreased to 1–4 ml/kg/hour (incomplete effectiveness) and stopped after 3–6 hours. In nine patients (12%) re-sternotomy was fulfilled because of ineffectiveness of rFVIIa therapy (bleeding rate 5 ml/kg/hour and more). Effectiveness of rFVIIa was higher in early administration of the drug (10–15 min after bypass). Following the hematology test, changes occurred: the APTT, INR and the SFMC concentration were decreased and the plasma FVIIa concentration was increased.

In group B life-threatening tracheal bleeding in mechanically ventilated septic patients with MOF was stopped in four of six cases (66.6%) during 30–75 min after rFVIIa administration. Both nonresponding patients were in severe uncorrectable respiratory/

metabolic acidosis before and during FVIIa infusion (pH 7.14/7.11, BE –12/–16 and pCO₂ 76/69 mmHg accordingly).

In group C the bleeding rate was decreased from 29 ± 12 ml/kg/hour to 4 ± 2.9 ml/kg/hour 2–5 hours after the second FVIIa infusion in six patients (66%). No cases of extracorporeal circuit/oxygenator thrombosis were occurred.

No significant adverse effects occurred in all groups.

Conclusion rFVIIa effectively prevents and treats bleeding in pediatric cardiac surgery, including life-threatening tracheal bleeding in septic patients and large blood loss during prolonged cardiopulmonary bypass with ECMO. Further research is required to determine the indications and dose regimens in these groups of patients.

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Cost-effectiveness analysis of recombinant activated factor VII as adjunctive therapy for bleeding control in severely injured trauma patients in Germany

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Introduction Uncontrollable bleeding is a leading cause of death in trauma patients and a major cause of preventable morbidity and mortality. Recombinant activated factor VII (rFVIIa) has been shown to decrease the need for red blood cell transfusion among severely injured blunt trauma patients. A significant difference in the incidence of acute respiratory distress syndrome was also observed relative to standard care together with a nonsignificant difference in mortality. While safety and efficacy of rFVIIa in trauma patients has been demonstrated, little is known about its cost-effectiveness.

Method The cost-effectiveness of rFVIIa relative to standard care was measured using patient-level data on survival and treatment patterns collected prospectively in a multicenter, international, trial, and outcomes data in the German Trauma Registry on patients matching key inclusion/exclusion criteria in the trial. Differences in survival observed at the end of trial and differences in healthcare cost were projected to a lifetime for each patient to produce an estimate of costs per life-year gained with rFVIIa. Analyses were conducted from the German third-party payer perspective, limited to healthcare costs and using a discount rate of 5%. The assessment considered adults with severe blunt trauma injury who had received 8 U RBC prior to random assignment to either three intravenous injections of rFVIIa (200, 100, and 100 µg/kg) or three placebo injections.

Results Projected to a lifetime, the mean cost per treated patient was €86,085 for rFVIIa and €65,875 for placebo, while life-years gained (LYG) were 13.17 and 12.22, respectively. The incremental cost of €21,210 and effect of 0.944 resulted in incremental costs per LYG of €21,410 for rFVIIa. Adjusting for quality of life (QoL) in residual life-years produced incremental quality-adjusted survival of 0.763 years and incremental costs per QALY gained of €26,502. Using a conservative threshold of €30,000 for cost-effective healthcare technologies, results appeared most sensitive to assumptions about residual life expectancy and QoL.

Conclusion rFVIIa is a cost-effective adjunctive therapy for control of bleeding in patients with severe blunt trauma injuries when compared with standard care in Germany.