Case Report

# Aortic Valve and Coronary Artery Bypass Surgery in a Patient with Factor VII Deficiency

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**ABSTRACT**

Congenital factor VII (FVII) deficiency is a rare bleeding disorder (RBD) with phenotypes ranging from asymptomatic state to life threatening bleeding episodes. There is no established recommendation for the perioperative management of patients scheduled for cardiac surgery. We have described the perioperative management of a patient with FVII deficiency treated for aortic valve stenosis, coronary artery disease, and atrial fibrillation. Balancing perioperative bleeding risk and risks of thrombotic events thereafter in such patients is difficult and requires a multidisciplinary approach.

**Keywords:** Cardiac surgery, FVII deficiency, rare bleeding disorders

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## INTRODUCTION

Rare bleeding disorders have an estimated prevalence of 0.5–2 in one million people.[1] Due to improved medical care and increased longevity numbers of patients with RBDs scheduled for surgery are rising. Cardiac surgery differs from other surgeries by usually involving heparin anticoagulation, hemodilution, and consumption of coagulation factors due to extracorporeal circulation (ECC) leading to multifactorial coagulopathy.

Congenital FVII deficiency represents about 39% of RBDs.[1] It is the most common autosomal recessive disorder and has a variable phenotype[1]: Some patients with low FVII activity do not bleed, whereas, others with similar levels bleed frequently.[2] Thrombotic events have been reported in 3-4% of patients with FVII deficiency.[1]

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## CASE PRESENTATION

The patient was a 69-year-old female with FVII deficiency due to mutations at exons 6 and 9 on chromosome 13. She had been treated with the vitamin K antagonist (VKA) Phenprocoumon for atrial fibrillation (AF) without any bleeding. FVII deficiency was diagnosed one year prior to cardiac surgery. On that occasion, Phenprocoumon was withheld for elective colonic polypectomy, but the international normalized ratio (INR) did not normalize. Further analysis showed a residual activity of FVII of only 7% (normal range 70–120%). Polypectomy was subsequently performed without bleeding complication with substitution of recombinant activated FVII (rFVIIa, Novoseven®, Novo Nordisk A/S, Denmark). Her bleeding history consisted of hypermenorrhagia leading to uterine abrasion at the age of 42 years followed



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by hemorrhage requiring hysterectomy. She reported no spontaneous bleeding episodes and had undergone minor surgeries uneventfully. Progressive dyspnea led to diagnosis of aortic valve stenosis and right coronary artery (RCA) stenosis. She was scheduled for elective cardiac surgery.

Because the type of cardiac surgery was considered as major surgery FVII activity was targeted to be at least 50% for the perioperative period by the hematologists. Plasma-derived FVII (Immuseven®, Baxalta GmbH, Germany) was chosen for substitution with the option of rFVIIa in case of bleeding emergency.

VKA was withheld five days prior to hospital admission. On admission day FVII activity (20%), INR (1.5), partial thromboplastin time (PTT) (25 sec.) and blood count were obtained. Challenge with plasma-derived FVII was performed by administering 1800 IU (about 20 IU/kg) to evaluate pharmacokinetics: FVII activity increased from 20% to 71% and declined to 39% four hours later, well corresponding to its half-life of about four hours [Figure 1].

On the day prior to surgery FVII activity was 25%. After administration of 2400 IU plasma-derived FVII on the morning of surgery FVII activity was 90%, INR was 0.98, activated clotting time (ACT) 121 sec. Before starting surgery 1800 IU of plasma-derived FVII were given additionally. With that FVII activity was estimated to remain at least at 50% for the duration of surgery (3.5 hours) based on results of presurgical plasma-derived FVII challenge protocol. Post-surgery FVII activity was confirmed to be 73%. Subsequent dosages were 2400 IE of plasma-derived FVII at 4 hours, then 1200 IE at 8 hours, 12 hours and 16 hours post-surgery. Further postoperative doses were adjusted based on these findings and FVII activity [Figure 1].

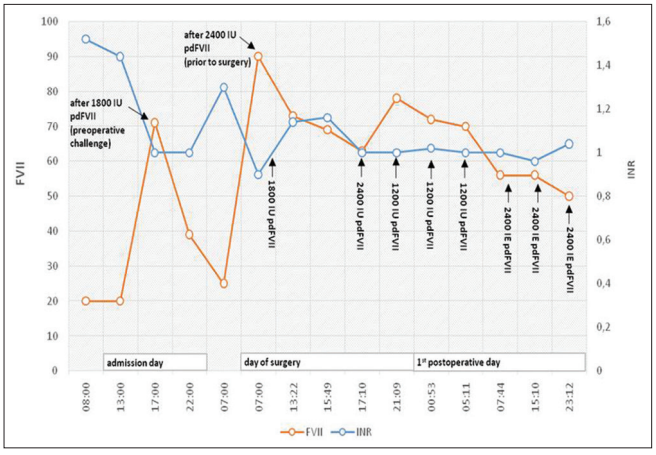


**Figure 1:** Monitoring of FVII activity (in %, normal range 70–120%) and INR (normal range 0,8 1,25) on admission day, day of surgery and 1st postoperative day. pdFVII: plasma derived factor VII; FVII: factor VII; INR: international normalized ratio

General anesthesia, placement of arterial line and central venous line were uneventful. After pericardiotomy 25000 IU of unfractionated heparin (UFH) were administered to achieve an ACT of 436 sec. Saphenous vein was grafted to the RCA, occlusion of left atrial appendage was performed, finally a 25 mm bioprosthetic valve (Perimount®, Edwards Life Sciences, Irvine CA) was implanted. At the end of surgery administering of 15000 IU of protamine hydrochloride resulted in an ACT of 102 sec. Weaning from ECC was uncomplicated. Intraoperative blood loss was 500 ml.

The patient was weaned off the respirator five hours post-surgery and transferred to the ward two days post-surgery. Anticoagulation with 8000 IU of UFH subcutaneously three times daily was resumed six hours post-surgery and continued for the duration of in-hospital stay. During the early postoperative period 1200 IU to 2400 IU of plasma-derived FVII were administered every six hours while monitoring the target range of FVII activity. The chest drain showed a total blood loss of 500 ml during the first 24 hours and was removed on 3rd postoperative day (POD). After removal of all catheters and pacemaker wire on 7th POD substitution of plasma-derived FVII was continued with a reduced dose until the 10th POD to ensure adequate wound healing. Blood transfusions were not necessary as serial blood counts showed a minimal hematocrit of 0.25 (normal range 0.35-0.47). The patient was discharged on 12th POD to a rehabilitation center. While anticoagulation with UFH subcutaneously was continued for three months after discharge, VKA was resumed with a target INR of 1.5 to 1.8 thereafter. Six-month follow-up was uneventful.

## DISCUSSION

Congenital FVII deficiency can be suspected with elevated INR, but normal PTT, if these changes are not explained by acquired factors.[1] The diagnosis is verified by reduced FVII activity, often far below 30%. Genetic testing is possible, but gene mutations are heterogeneous.[2] Unlike in hemophilia there is a lack of correlation between FVII activity and bleeding risk.[2] As a consequence and because of the rarity of the disease established recommendations for perioperative management of patients with FVII deficiency do not exist. Therefore, replacement therapy is challenging and must be individualized per case basis.[2]

Several replacement options are available: fresh frozen plasma and prothrombin complex concentrate contain

low amounts of FVII, whereas rFVIIa and plasma-derived FVII are specific products.[2,3] An analysis of the database of the Seven Treatment Evaluation Registry published in 2018 included 113 patients, of whom 95 were treated with rFVIIa for 110 surgical procedures (among those two cardiac surgical procedures, not further specified).[4] Only 16 patients received plasma-derived FVII and were not included in the detailed analysis.[4] rFVIIa consists of activated FVII (1-3% of total FVII in physiological condition) and promptly activates coagulation. There are reports of thromboembolism caused by application of rFVIIa in patients with FVII deficiency.[4,5] Because for cardiac surgery heparin anticoagulation is necessary during ECC plasma-derived FVII seemed the better choice.

Though FVII activity above 20% is described to protect from spontaneous bleeding,[6] FVII activity above 50% seemed reasonable in this patient for major surgery with additional perioperative interventions. Due to the short half-life of FVII replacement was necessary several times daily. Whether a lower target range would have been equally safe can only be speculative.

The presented case demonstrates the feasibility and safety of a complex cardiac surgery in a patient with FVII deficiency. Baseline factor activity, bleeding history, and type of surgery all play an important role in the decision of the appropriate management strategy. Multidisciplinary planning of the procedure involving cardiologists, anesthesiologists, and hematologists is essential. As RBDs show a low prevalence, studies on perioperative management are not feasible. The number of affected patients with indication for cardiac surgery is even smaller but will increase due to better diagnostic and therapeutic options. Collection of case reports and registry databases are required to improve knowledge in the management of RBDs.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Authors contributions**

LH and CJ have done the patient follow-up over the years and helped draft the manuscript.

AO have performed preoperative diagnostics and helped draft the manuscript.

PMD and AA have drafted the manuscript and performed the surgery.

**Disclosures**

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All other Authors have no conflict of interest to declare.

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There are no conflicts of interest.

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