

## Summary Comment to: “Severe Perioperative Bleeding in Renal Cell Carcinoma after Elective Pericardiocentesis Associated Left Ventricular Puncture: Case Report”

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Dear Sir,

After the publication of our work “Severe Perioperative Bleeding in Renal Cell Carcinoma after Elective Pericardiocentesis Associated Left Ventricular Puncture: Case Report”, we have received comments from our coworkers and colleagues at other institutions in reference to our approach in this difficult case [1]. Sharing the experiences of surgical and anesthetic teams when facing adverse situations in the management of cancer patients can help health professionals to better understand the complexity of pathophysiologic processes and the course of action that could benefit the patient. In this letter, we want to highlight the most relevant aspects discussed in this article as well as give a concise message that, hopefully, can help in the management of cancer patients in this particular situation.

The 5 years survival rate of patients with renal cell carcinoma taken to radical nephrectomy can drop dramatically (by 40%) if distant metastases are present [2]. Complications can arise at any point of treatment, some of them being very serious. In the case mentioned, a puncture of the left ventricle presented after pericardiocentesis, which is rare, but potentially lethal [3]. Given that, the left ventricle has a higher pressure and is anatomically more difficult to access than its counterpart, the right ventricle.

Several studies have found that coagulation disorders in cancer patients can present in different forms, ranging from hemorrhage to thrombotic events. Patients with cancer are at higher risk of severe bleeding and coagulopathy during major surgery [4]. These coagulation disorders can occur at any point of surgical management (pre-, intra- and post-operatively).

In addition to the oncologic status, our patient was also complicated by the risks of cardiothoracic surgery, such as severe bleeding and potential need for transfusion of blood products; as well as those derived from sepsis and liver failure.

At the onset of the case laboratory tests showed an activated partial thromboplastin time (aPTT) of 195.1 s, (reference, 24.7-35.9), prothrombin time (PT) of 20 s (reference, 12.7-15.0), international normalized ratio (INR) of 1.73 (reference, 0.9-1.20), hemoglobin level (Hb) of 9.3 g/dL and platelet count of 305 k/uL. The patient's vital signs were as follows: blood pressure (BP): 130/80 mmHg; heart rate (HR): 110 beats per min; respiratory rate (RR): 20 respirations per min; and temperature: 37°C.

After the incision was closed, the patient continued to lose blood: an estimated 3 L of blood was collected from the chest tubes over a period of 20 min. The anesthesia team managed bleeding and coagulopathy with standard blood products and fluids [5]. The blood and blood products used were 9 units of red blood cells, 12 units of fresh frozen plasma, 2 6-pack platelet units and 2 10-units cryoprecipitate. Fluids administered included 500 mL 5% albumin. FloTrac/Vigileo (Edwards Lifesciences, Irvine, CA) minimally invasive hemodynamic monitoring was used for goal directed fluid therapy.

Because the bleeding had not stopped 20 min after closure of the incision, the surgeons considered reopening the incision and conducting further exploration, but they refrained from doing so, as the patient might not have tolerated a sound procedure. The chest tubes continued to ooze blood, indicating a partial lack of response to the use of blood derivatives, so the anesthesia team decided to administer 10 mg NovoSeven recombinant factor VIIa (rFVIIa) (Novo Nordisk A/S, Bagsvaerd, Denmark) [6]. This dose was calculated based on a dosing of 90 mcg/kg IV bolus for a severe bleeding episode. Ten min after the administration of rFVIIa, the blood loss was significantly reduced, with only an additional 200 mL collected over the next 30 min. The total estimated blood loss was 5.5 L. Laboratory tests right at the end of surgery showed the following results: activated partial thromboplastin time (aPTT), 30 s; prothrombin time (PT), 10 s; international normalized ratio (INR), 0.68; hemoglobin (Hb), 9.5 g/dL; platelet count 184 k/uL and fibrinogen, 433 mg/dL (reference, 202-450).

Recombinant factor VIIa (rFVIIa) was used successfully in this case when therapy with conventional blood products failed. Even though, some authors have discussed the off-label use of rFVIIa, there is no sufficient evidence of its safety and efficacy, and there is even less information about the off-label use in cancer patients. Special consideration should be taken with the potential increase of thrombotic events after the administration of rFVIIa. In this particular case, the use of the medication resulted in a successful outcome. Nevertheless, decisions must be taken individually for each patient, pondering the risks and potential benefits of any therapy. In addition to patients coagulopathy and underlying malignancy and its effect on hemostasis/fibrinolysis the patient given his critically ill presentation also had liver and renal impairment, further affecting to his coagulopathy and leading to post-operative hemorrhage; liver function and kidney function prior to procedure was as follows: Preoperative Aspartate transaminase level (AST) of 77 IU/L (reference, 15-46 IU/L), alanine transaminase level (ALT) of 366 IU/L (reference, 7-56 IU/L), total bilirubin of 2.1 mg/dL (reference, 0.2-1.3 mg/dL), albumin 3 g/dL (reference, 3.5-4.7 g/dL) and creatinine 7.63 mg/dL Further investigation should be done to clarify the role of rFVIIa in the management of severe perioperative bleeding in cancer patients [7].

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Post-operatively, the patient was managed in the intensive care unit for 9 days, where he steadily improved, vasopressor support was discontinued, and he was weaned off mechanical ventilation and underwent intermittent hemodialysis [8]. The patient showed no signs of coagulopathy during the rest of his hospitalization. Having experienced no other complications, he was discharged to a long-term acute care facility 24 days after surgery, where management of his condition continued.

Patients with cancer are often challenging, therefore, we recommend a multidisciplinary and comprehensive cancer care approach. Anesthetic and surgical teams must be prepared to manage these situations along with the arising complications of the disease and treatment.

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