Turkish Journal of Thoracic and Cardiovascular Surgery 2025;33(2):251-256

Case Report / Olgu Sunumu

Is it safe to perform coronary artery bypass grafting surgery in patients with hemophilia? A case series of four patients

Hemofili hastalarında koroner arter baypas greftleme ameliyatı uygulamak güvenli midir? Dört hastadan oluşan vaka serisi

Fatoş Dilan Köseoğlu[1], Zühal Demirci[2], Ümit Kahraman[3], Güray Saydam[2], Fahri Şahin[2]

Institution where the research was done:
Ege University Faculty of Medicine, İzmir, Türkiye

Author Affiliations:
[1]Department of Internal Medicine, Division of Hematology, Bakırçay University Faculty of Medicine, İzmir, Türkiye
[2]Ege University Hospital, Thrombosis and Hemostasis Center, İzmir, Türkiye
[3]Department of Cardiovascular Surgery, Ege University Faculty of Medicine, İzmir, Türkiye

ABSTRACT

Hemophilia is a genetic disorder that mainly affects males and leads to a higher risk of bleeding. There is a lack of clarity regarding the safety of coronary artery bypass grafting (CABG) surgery in patients with hemophilia. In this case series, real-life data of four male hemophilia patients aged 45 to 66 years who underwent CABG was presented. One patient needed to undergo reexploration due to nonsurgical bleeding. However, all patients were discharged in good condition. The current experience revealed that CABG in hemophilia patients is safe to perform with a multidisciplinary approach involving hematologists, anesthesiologists, and cardiovascular surgeons.

Keywords: Cardiovascular disease; coronary artery bypass grafting; hemophilia; surgery.

ÖZ

Hemofili, esas olarak erkekleri etkileyen ve kanama riskini artıran genetik bir bozukluktur. Hemofili hastalarında koroner arter baypas greftleme (KABG) ameliyatının güvenliği net değildir. Bu olgu serisinde, KABG uygulanan 45 ile 66 yaşları arasındaki dört erkek hemofili hastasının gerçek yaşam verileri sunuldu. Ameliyet harici kanama nedeniyle bir hastada yeniden eksplorasyon gerekti. Ancak tüm hastalar iyi durumda taburcu edildi. Bu deneyim; hematologlar, anesteziyologlar ve kardiyovasküler cerrahlar dahil olmak üzere multidisipliner bir yaklaşım ile hemofili hastalarında KABG'nin güvenle gerçekleştirilebileceğini ortaya koydu.

Anahtar sözcükler: Kardiyovasküler hastalıklar, koroner arter baypas greftleme, hemofili, cerrahi.

Hemophilia is an X-linked recessive inherited disease affecting primarily males, with females predominantly serving as carriers. Two major types, Hemophilia A and B, are characterized by factor VIII and IX deficiencies, respectively.[1] In the last decade, the medical community has witnessed remarkable advancements in developing new factor VIII/IX concentrates that have significantly improved the treatment of patients with hemophilia. These concentrates have drastically improved the life expectancy of hemophilia patients, enabling them to lead longer and healthier lives.[2] Cardiovascular diseases (CVDs) are the leading cause of death worldwide among adults. Patients with hemophilia have a similar prevalence of CVD to the general population of similar age.[3] This has presented a new challenge regarding how to approach patients with hemophilia who need high-risk surgery for bleeding, such as coronary artery bypass grafting (CABG).[4] Herein, we sought to share the positive outcomes of CABG surgeries conducted with a multidisciplinary approach in four cases of hemophilia.

Corresponding author: Fatoş Dilan Köseoğlu.
E-mail: fatosdilankoseoglu@gmail.com

Doi: 10.5606/tgkdc.dergisi.2025.25800

Received: November 30, 2023
Accepted: March 10, 2024
Published online: April 30, 2025

Cite this article as: Dilan Köseoğlu F, Demirci Z, Kahraman Ü, Saydam G, Şahin F. Is it safe to perform coronary artery bypass grafting surgery in patients with hemophilia? A case series of four patients. Turk Gogus Kalp Dama 2025;33(2):251-256. doi: 10.5606/tgkdc.dergisi.2025.25800.

Table 1. Demographics and periprocedural details of the patients

	Case 1	Case 2	Case 3	Case 4
Demographics				
Age (year)	45	66	57	60
Sex	Male	Male	Male	Male
Weight (kg)	86	95	90	100
Type of hemophilia	Hemophilia B	Hemophilia A	Hemophilia A	Hemophilia A
Severity of hemophilia	Mild	Mild	Severe	Mild
Factor level at the time of diagnosis (IU/dL)	FIX: 8.7	FVIII: 16.4	FVIII: 0.4	FVIII: 11.4
Presence of inhibitor	Negative	Negative	Negative	Negative
Clinical presentation	Elective	Elective	Elective	Elective
Indication for CABG	Chronic total occlusion in proximal RCA, critical LCx mid and LAD proximal lesion	Distal left main coronary artery and ostial LAD lesions	Chronic total occlusion in RCA and LCx, critical lesion in LAD mid-region	Critical multivessel disease with diabetes
Operation details	On-pump CABG Three grafts (LIMA-LAD, Ao-saphenous vein-RCA, Ao-saphenous vein-OM1) were used.	Off-pump CABG Three grafts (LIMA-LAD, Ao-saphenous vein-diagonal artery 1, Ao-saphenous vein-OM1) were used.	On-pump CABG Three grafts (LIMA-LAD, Ao-saphenous vein-RCA, Ao-saphenous vein-OM2) were used.	On-pump CABG Four grafts (LIMA-LAD, Ao-saphenous vein-diagonal artery 1, Ao-saphenous vein-RCA, Ao-saphenous vein-OM1) were used.
LVEF (by echocardiogram)	55%	60%	40%	58%
Valve disease	Mild tricuspid and mitral regurgitation	None	Mild-to-moderate mitral regurgitation and mild tricuspid regurgitation	Mild mitral regurgitation
Comorbidities	HT, COPD	HT	Heart failure	DM
Smoking history	15 pack-years	25 pack-years	None	None
Preoperative hemogram				
Hemoglobin (g/dL)	14.9	14.0	14.7	15.1
Hematocrit (%)	43.8	42.5	45.2	44.1
Platelet ($\times 10^3/\mu L$)	263	291	259	234
Procedural management				
Preoperative factor level target (%)	100	100	100	100
Factor replacement	1000 IU FIX for every 1000 mL blood loss.	500 IU FVIII for every 1000 mL blood loss.	500 IU FVIII for every 1000 mL blood loss.	500 IU FVIII for every 1000 mL blood loss.
Post-procedural care				
Immediate postoperative	FIX level and ACT were requested.	FVIII level and ACT were requested.	FVIII level and ACT were requested.	FVIII level and ACT were requested.
1-3th days	The target factor level was kept at 80% and reduced to 50% on 3rd day. Additional doses can be given in case of bleeding.	The target factor level was kept at 80%.	The target factor level was kept at 100% (there was bleeding, so two units of red cell transfusion were given)	Post-op 1st day: Hematocrit level reduced to 27.1%, so two units of red cell transfusion were given. The target factor level was maintained at 100% until bleeding was controlled (till post-op 2nd day). The hemogram and ACT were monitored twice daily.

Table 1. Continued

	Case 1	Case 2	Case 3	Case 4
4-6th days	The target factor level was kept at 50%.	The target factor level was kept at 60%.	The target factor level was kept at 70-80 %.	The factor level was kept at 70-80%. Daily 500 IU was suggested for patients who continued with ASA without bleeding.
7-9th days	The target factor level was kept at 30%.	The target factor level was held at 40%.	The target factor level was kept at 40%.	The target factor level was kept at 50%.
10-14th days	The target factor level was kept at 20%.	The target factor level was held at 20%.	The target factor level was maintained at 30%.	The target factor level was kept at 30%.
1st-month follow-up	The target factor level was kept at 20%.	The target factor level was kept at 20%.	The target factor level was kept at 30%.	The target factor level was kept at 20%.
3rd-month follow-up	The target factor level was kept at 20%.	The target factor level was kept at 20%.	The target factor level was kept at 30%.	The target factor level was kept at 20%.
Complications	None	None	Minor bleeding	Major bleeding
Management of complication	-	-	Observation	Surgical re-exploration
Tube drainage (mL)	550	850	950	1000 (1300 after re-exploration)
Transfusions (unit)				
ES	1	4	5	4
PS	0	0	1	0
FFP	3	6	5	5
CP	0	0	6	6
ICU length of stay (day)	1	1	2	3
Length of hospitalization (day)	11	14	12	20

FIX: Factor IX; RCA: Right coronary artery; LCx: Circumflex artery; LAD: Left anterior descending artery; CABG: Coronary artery bypass grafting; LIMA: Left internal mammarian artery; OM: Obtuse marginal artery; Ao: Aorta; LVEF: Left ventricular ejection fraction; HT: Hypertension; COPD: Chronic obstructive pulmonary disease; DM: Diabetes mellitus; ACT: Activated clotting time; ASA: Acetylsalicylic acid; ES: Erythrocyte suspension; PS: Platelet suspension; FFP: Fresh frozen plasma; CP: Cryoprecipitate; ICU: Intensive care unit.

CASE REPORT

Case 1- A 45-year-old male with mild haemophilia B underwent elective on-pump CABG for chronic total occlusion of the proximal RCA, critical mid-LCx and proximal LAD lesions. Three grafts were used: LIMA to LAD, ao-saphenous vein to RCA and ao-saphenous vein to OM1. The patient's preoperative hemoglobin was 14.9 g/dL and his hematocrit was 43.8%, with a platelet count of 263×10^3 µL. Factor IX was administered at 1000 IU per 1000 mL blood loss. Postoperative care was aimed at maintaining factor levels at 80%, which was reduced to 50% by Day 3, with no reported complications. The patient's ICU stay was one day, with a total hospital stay of 11 days. A written informed consent was obtained from the patient.

Case 2- A 66-year-old male with mild hemophilia A and a history of hypertension and COPD underwent off-pump CABG for distal left main and ostial LAD lesions using three grafts: LIMA to LAD, ao-saphenous vein to diagonal artery 1, and ao-saphenous vein to OM1. With a preoperative hemoglobin of 14.0 g/dL and hematocrit of 42.5%, factor VIII was administered at 500 IU per 1000 mL blood loss. Postoperative care was aimed at achieving a factor level of 80% and no complications were observed. ICU and hospital stays were one and 14 days respectively. A written informed consent was obtained from the patient.

Case 3- The third case was a 57-year-old male with severe haemophilia A. The patient underwent on-pump CABG for chronic total occlusions in the RCA and LCx and a critical lesion in the mid LAD. Three grafts were used: LIMA to LAD, ao-saphenous vein to RCA and ao-saphenous vein to OM2. Preoperatively, the patient had a hemoglobin of 14.7 g/dL, a hematocrit of 45.2% and a platelet count of 259×10^3 µL. Despite a target of 100% factor due to bleeding, which required two units of erythrocyte transfusion, minor bleeding was

managed conservatively. The patient spent two days in intensive care and 12 days in hospital. A written informed consent was obtained from the patient.

Case 4- A 60-year-old male with mild haemophilia A and diabetes required on-pump CABG for critical multivessel disease. Four grafts were used: LIMA to LAD, ao-saphenous vein to diagonal artery 1, ao-saphenous vein to RCA and ao-saphenous vein to OM1. Preoperative hemoglobin was 15.1 g/dL, hematocrit was 44.1% and platelet count was 234×10^3 μL. Factor VIII was administered at 500 IU per 1000 mL blood loss. Surgical re-exploration was required due to significant bleeding. Postoperative care included maintaining factor levels at 70-80% with daily monitoring. The patient spent three days in intensive care, with a total hospital stay of 20 days. A written informed consent was obtained from the patient.

Factor VIII or IX levels were checked preoperatively. The surgical procedure was conventional CABG by median sternotomy with cardiopulmonary bypass (CPB). Unfractionated heparin was administered based on patients' weight (mean weight: 400 IU/kg) to achieve adequate anticoagulation during CPB. The target activated clotting time (ACT) level was 480 sec. throughout CPB, repeated every 30 min. During surgery, various techniques were used to control bleeding, such as electrocautery, absorbable hemostatic materials, and fibrin sealant. Factor levels, activated partial thromboplastin time, and ACT were closely monitored in the immediate postoperative period. Every 1000 mL of blood lost was replaced with 500 IU of factor VIII or 1000 IU of factor IX. Factor levels were gradually reduced after surgery. Plasma levels of factor VIII and IX were measured using a one-stage clot-based factor assay. All patients were screened for factor VIII or factor IX inhibitors using the Bethesda method prior to surgery.[6,7] Due to limitations in accessibility, factor levels were not evaluated daily or postoperatively. Our institution provided factor-level results within seven to 10 days. Daily ACT and clinical bleeding were closely monitored to ensure patient safety. The development of factor inhibitors, which are antibodies that block the blood clotting function, is a significant complication of hemophilia treatment.[7] These antibodies can also cause bleeding in healthy individuals who develop autoimmune antifactor antibodies, although this is rare. All patients were screened for inhibitors to factor VIII or factor IX in case of developing factor inhibitors due to exposure to a high amount of clotting factor concentrates. None of our patients developed inhibitors after the operation.

In terms of medical complications, one patient required a surgical reexploration due to noteworthy mediastinal bleeding. The reexploration identified minor bleeding areas from the sternum and its wires, which were skillfully resolved. The duration of hospitalization in the intensive care unit was between one to three days. All patients were discharged after a total hospitalization period ranging from 11 to 20 days.

DISCUSSION

This series presents encouraging results for patients with hemophilia who require elective CABG surgery and highlights the critical importance of tailored haemostatic and surgical strategies in the management of haemophilia patients undergoing CABG. Patients presented with a range of haemophilia severity. Pre-operative preparation included careful screening for factor VIII or IX levels and inhibitors, followed by conventional CABG with cardiopulmonary bypass. Unfractionated heparin, dosed according to patient weight and target ACT levels, ensured adequate anticoagulation. Bleeding control during surgery was achieved using electrocautery, absorbable haemostatic materials and fibrin sealant, with factor replacement tailored to blood loss and closely monitored postoperatively. After surgery, factor levels were carefully adjusted over days and weeks to reduce the risk of bleeding while promoting healing. Despite rigorous management, one patient experienced significant mediastinal bleeding requiring surgical re-exploration, highlighting the complexity of managing haemophilia in major surgery. Hospital stays ranged from 11 to 20 days.

This study presents encouraging results for patients with hemophilia who require elective CABG surgery. The study evaluated four patients, including one with severe hemophilia. It demonstrated that a multidisciplinary approach to the management of these patients is effective in minimizing complications during and after the surgery. These results may open a new horizon in the approach to hemophilia patients in need of elective CABG surgery to prevent avoiding surgical intervention in daily practice.

Cardiac surgery in hemophilia patients is considered high risk, mainly due to the complications associated with bleeding. Several reports highlight the success of a multidisciplinary approach to this group of patients. Most are case reports with limited patients.[8-12] One of the most extensive

literature searches was done by Kanellopoulou and Nomikou,[13] including 43 cases of hemophilia requiring cardiac surgery. Over half were mild or asymptomatic carriers, and preoperative treatments mainly targeted normalizing factor VIII or factor IX levels using plasma-derived or recombinant factor concentrates. The survival rate was 95%. No complications were reported in 30 cases. Among others, the most devastating complication was aortic dissection in one case.[14] Another case series of hemophilia was derived from the Danish Heart Database by Tang et al.[15] In this report, perioperative management included tranexamic acid in the first 6 to 10 days postoperatively. Excellent results have been achieved, including no reexploration for bleeding, no fresh frozen plasma use, and no severe complications. Furthermore, similar postoperative outcomes were found when compared with patients without hemophilia.[15] Lin and Yao[16] conducted a meta-analysis of 50 studies reported on 72 hemophilia patients requiring cardiac surgery. In this group, only 35% of all patients had severe hemophilia A, and seven patients had factor VIII inhibitors, which can complicate the treatment strategy. This analysis revealed that although an uneventful clinical outcome was achieved in the majority of cases, 20% of patients developed complications with different severities. However, the complications experienced by one in five patients underscore the importance of continued research and refined management strategies to optimize surgical outcomes in this particular patient group.

A comprehensive stepwise guide for managing patients with hemophilia during the perioperative period was reported by Kwak et al.[17] The authors point out the multidisciplinary approach, timing of essential tests, optimization of factor levels, perioperative administration of antifibrinolytics, blood conversation techniques during CPB, and, finally, optimal management of antithrombotic treatments in the postoperative period. However, there are concerns about the lack of high-quality evidence and the possible impact of publication bias on this subject. Kwak et al.[17] concluded that poor surgical outcomes may not have been reported. Another significant point was the potential risk of exposure to factor concentrates early in life, predisposing severely affected hemophiliac patients to the development of inhibitors. Nevertheless, positive outcomes are conceivable for this specific patient subgroup, provided the correct procedures and precautions are employed. Key recommendations from this topic emphasized a collaborative team approach, a clear factor replacement protocol, and meticulous perioperative monitoring of factor levels.[18]

In high-income countries, where access to coagulation factors is readily available, personalized treatment protocols are often implemented through pharmacokinetic assessment and closely monitoring factor levels. However, in resource-limited settings, frequent assessment of factor levels may not be feasible. Instead, specific measures such as ACT and clinical signs of bleeding have to be used. These limitations were also true for this series; nevertheless, satisfactory outcomes were achieved in the patients with hemophilia during CABG through the expertise of our surgery and vigilant oversight by hematologists. The statement implies that a patient's cardiovascular health can still be enhanced, even in cases where there is inadequate monitoring available. This can be achieved through a multidisciplinary approach, where a team of experts from different fields work together to devise a comprehensive plan for the patient's care. Such an approach can potentially make up for the lack of optimal monitoring, resulting in better outcomes for the patient's cardiovascular health.

Recent studies on hemophilia patients have shown that they have a similar rate of CVD as the general population.[3] However, managing CVD in hemophilia patients can be challenging for physicians due to the need for antiaggregant, anticoagulant, and, sometimes, thrombolytic therapy. To address this issue, current recommendations suggest that managing antiaggregant and anticoagulant therapy in hemophilia patients should be similar to nonhemophilic patients. In cases where individuals suffer from severe hemophilia or require long-term antithrombotic treatment, it is important to administer prophylaxis measures. This is crucial when there is a high risk of bleeding due to other underlying medical conditions. By taking such precautions, we can effectively manage potential complications and promote better health outcomes.[19]

There are a few limitations to this case series that should be noted. First, despite the small sample size of our study, we believe that it still provides valuable results for hemophilic patients with CVD, given the prevalence of hemophilia in the community. Second, all of the cases that were operated on were elective surgeries, so the data may not be as accurate for patients who require emergency or urgent CABG operation after an acute coronary syndrome. Third, it is essential to note that the cases were in the young or middle-aged group, and we did not have any cases aged 75 years or older. Therefore, we cannot draw any

conclusions about how the results may differ in elderly hemophilic patients. In addition, the lack of a cell saver and the lack of ideal laboratory facilities may be a limitation of this study.

In conclusion, the findings of this case series demonstrate that hemophilia patients with cardiovascular diseases who require coronary artery bypass grafting surgery can undergo elective surgery safely, provided they receive vigilant factor level monitoring and a multidisciplinary approach. This case series highlights the possibility of cardiac surgery for hemophilia patients, despite limited research in this area. However, to establish a more conclusive understanding of this matter, larger multicenter investigations in big university or city hospitals are necessary to validate our results.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Designed the article: F.D.K.; Collected the data: F.D.K., Z.D., Ü.K.; Reviewed literature: F.D.K., Z.D.; Writed the article: F.D.K., Ü.K.; Made critical review: G.S., F.S.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Bolliger D, Vandyck K, Tanaka KA. Management of patients with hemophilia undergoing cardiac surgery. J Cardiothorac Vasc Anesth 2022;36:539-41. doi: 10.1053/j.jvca.2021.11.022.
2. Morfini M, Rapisarda CAP. Safety of recombinant coagulation factors in treating hemophilia. Expert Opin Drug Saf 2019;18:75-85. doi: 10.1080/14740338.2019.1574743.
3. White GC 2nd, Rosendaal F, Aledort LM, Lusher JM, Rothschild C, Ingerslev J; Factor VIII and Factor IX Subcommittee. Definitions in hemophilia. Recommendation of the scientific subcommittee on factor VIII and factor IX of the scientific and standardization committee of the International Society on Thrombosis and Haemostasis. Thromb Haemost 2001;85:560.
4. Bhave P, McGiffin D, Shaw J, Walsh M, McCarthy P, Tran H, et al. Guide to performing cardiac surgery in patients with hereditary bleeding disorders. J Card Surg 2015;30:61-9. doi: 10.1111/jocs.12464.
5. Berntorp E, Fischer K, Hart DP, Mancuso ME, Stephensen D, Shapiro AD, et al. Haemophilia. Nat Rev Dis Primers 2021;7:45. doi: 10.1038/s41572-021-00278-x.
6. Millner AH, Tiefenbacher S, Robinson M, Boesen HT. A variation of the Nijmegen-Bethesda assay using heat or a novel heat/cold pretreatment for the detection of FIX inhibitors in the presence of residual FIX activity. Int J Lab Hematol 2016;38:639-47. doi: 10.1111/ijlh.12552.
7. Tiede A, Collins P, Knoebl P, Teitel J, Kessler C, Shima M, et al. International recommendations on the diagnosis and treatment of acquired hemophilia A. Haematologica 2020;105:1791-801. doi: 10.3324/haematol.2019.230771.
8. Odonkor P, Srinivas A, Strauss E, Williams B, Mazzeffi M, Tanaka KA. Perioperative coagulation management of a hemophilia a patient during cardiac surgery. Semin Cardiothorac Vasc Anesth 2017;21:312-20. doi: 10.1177/1089253217702747.
9. Xu H, Henry D, Li C, Zhao H, Yang Y. Peri-cardiac surgery coagulation management in a severe hemophilia A patient: A case report. Medicine (Baltimore) 2019;98:e15897. doi: 10.1097/MD.0000000000015897.
10. Kang MY, Wang JD, Wei HJ. Gene therapy and cardiac surgery in a patient with hemophilia. JTCVS Tech 2022;16:102-4. doi: 10.1016/j.xjtc.2022.08.028.
11. Bohn JP, Fiala A, Bachmann S, Irsara C, Wolf D, Feistritzer C. Major cardiac surgery with recombinant FIX Fc fusion protein replacement in hemophilia B: A case report. Ther Adv Hematol 2022;13:20406207221104595. doi: 10.1177/20406207221104595.
12. Shalabi A, Kachel E, Kogan A, Sternik L, Grosman-Rimon L, Ben-Avi R, et al. Cardiac surgery in patients with Hemophilia: Is it safe? J Cardiothorac Surg 2020;15:76. doi: 10.1186/s13019-020-01123-0.
13. Kanellopoulou T, Nomikou E. Replacement therapy for coronary artery bypass surgery in patients with hemophilia A and B. J Card Surg 2018;33:76-82. doi: 10.1111/jocs.13530.
14. Donahue BS, Emerson CW, Slaughter TF. Case 1--1999. Elective and emergency cardiac surgery on a patient with hemophilia B. J Cardiothorac Vasc Anesth 1999;13:92-7. doi: 10.1016/s1053-0770(99)90181-7.
15. Tang M, Wierup P, Terp K, Ingerslev J, Sørensen B. Cardiac surgery in patients with haemophilia. Haemophilia 2009;15:101-7. doi: 10.1111/j.1365-2516.2008.01895.x.
16. Lin PS, Yao YT. Perioperative management of hemophilia a patients undergoing cardiac surgery: A literature review of published cases. J Cardiothorac Vasc Anesth 2021;35:1341-50. doi: 10.1053/j.jvca.2020.06.074.
17. Kwak J, Mazzeffi M, Boggio LN, Simpson ML, Tanaka KA. Hemophilia: A review of perioperative management for cardiac surgery. J Cardiothorac Vasc Anesth 2022;36:246-57. doi: 10.1053/j.jvca.2020.09.118.
18. Rossi M, Jayaram R, Sayeed R. Do patients with haemophilia undergoing cardiac surgery have good surgical outcomes? Interact Cardiovasc Thorac Surg 2011;13:320-31. doi: 10.1510/icvts.2011.272401.
19. Franchini M, Focosi D, Mannucci PM. How we manage cardiovascular disease in patients with hemophilia. Haematologica 2023;108:1748-57. doi: 10.3324/haematol.2022.282407.