

complications. A switch to a short-term LVAD is feasible within the Spanish heart transplant program.

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Short-term Heparin Re-exposure During Heart Transplantation in Patients With Ventricular Assist Devices and Acute Heparin-induced Thrombocytopenia



Reexposición temprana a heparina durante el trasplante cardíaco de pacientes con trombocitopenia inducida por heparina y asistencia ventricular

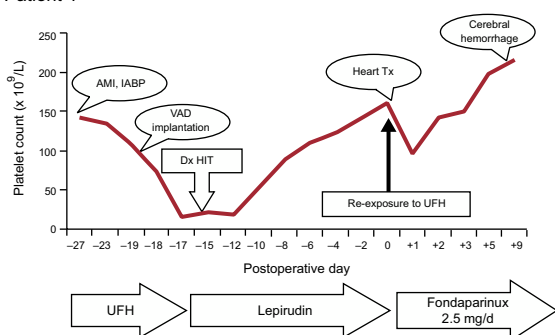
To the Editor,

The increasing use of ventricular assist devices as a bridge to heart transplantation improves survival in candidates for

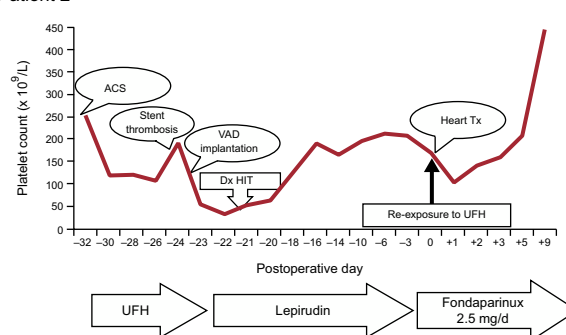
transplantation. Intravenous unfractionated heparin (UFH) is routinely used to prevent the thromboembolic complications associated with the pump and support cannulae. Occasionally, UFH can trigger a specific immunological response, characterized by the development of antibodies against UFH/platelet factor 4 complex, activating platelets, and leading to heparin-induced thrombocytopenia (HIT). In such cases, UFH must be switched to an alternative anticoagulation, usually parenteral direct thrombin inhibitors.¹

After 3 months, anti-UFH/platelet factor 4 antibodies are usually undetectable, and the risk of recurrent HIT on re-exposure to heparin is reduced. For patients with acute or subacute HIT requiring cardiopulmonary bypass (CPB) surgery, clinical

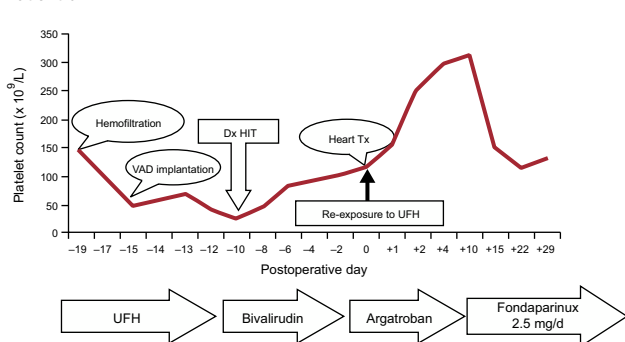
Patient 1



Patient 2



Patient 3



Patient 4

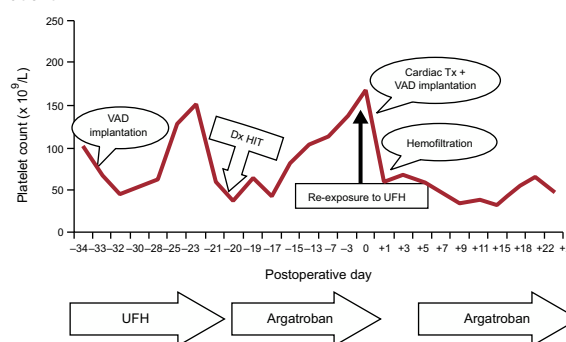


Figure. Trends in platelet count. ACS, acute coronary syndrome; AMI, acute myocardial infarction; Dx HIT, diagnosis of heparin-induced thrombocytopenia; IABP, intra-aortic balloon pump; Tx, transplant; UFH, unfractionated heparin; VAD, ventricular assist device.

Table
Summary of Patient Characteristics

Patient	Age, years	Sex	Indication for transplantation	Type of VAD	Platelet count on placing VAD, $\times 10^9/L$	Lowest platelet count, $\times 10^9/L$	Start UFH-Dx HIT, days	Start VAD-Dx HIT, days	4Ts score	pre-Tx alternative anticoagulation	Dx HIT-transplantation, days	Platelet count at transplantation, $\times 10^9/L$	Anti-UFH/ PF4 at transplantation	Posttransplantation anticoagulation	Outcome
1	62	F	Cardiogenic shock secondary to ACS	Left	82	15	10	2	4	Lepirudin	18	161	+	Fondaparinux	Died (day +8) secondary to CNS hemorrhage
2	52	M	Cardiogenic shock secondary to ACS	Bilateral	54	32	10	2	5	Lepirudin	21	170	+	Fondaparinux	Alive at 50 months post-Tx
3	48	M	End-stage HF secondary to dilated cardiomyopathy	Bilateral	154	25	8	5	5	Bivalirudin	10*	116	+	Argatroban, fondaparinux	Alive at 24 months post-Tx
4	62	F	Cardiogenic shock secondary to ACS	Bilateral	68	36	13	13	5	Argatroban	20	168	+	Argatroban	Died (day +27) to fungal sepsis

ACS, acute coronary syndrome; CNS, central nervous system; Dx HIT, heparin-induced thrombocytopenia; F, female; HF, heart failure; M, male; Tx, transplantation; VAD, ventricular assist device.
* Cardiorenal transplantation.

guidelines recommend delaying surgery, when possible, until the disappearance of antibodies, and then using UFH again. If surgery cannot be delayed, a different anticoagulant can be used (grade 2C).¹ However, patients with HIT who have short-term ventricular assist devices cannot wait for the antibodies to disappear. Therefore, the treatment of these patients presents a clinical challenge. In the case of CPB, early re-exposure to UFH can make HIT worse. However, there is limited experience with the use of direct thrombin inhibitors during CPB, and a significant increase in hemorrhage has been described, due to the complexity of intra-operative monitoring of the anticoagulant effect and the lack of antidotes.²

We describe our experience with 4 patients who required a ventricular assist device (Levitronix Centrimag) due to acute heart failure and who developed HIT and underwent transplantation using UFH within a few weeks.

Patient characteristics and trends in platelet counts are summarized in the [Table](#) and in the [Figure](#), respectively. A more detailed description of each case is provided in the [supplementary material](#).

According to the 4Ts score,¹ all patients had at least an intermediate pretest clinical probability of HIT. All patients had positive determination of anti-UFH/PF4 antibodies on particle gel immunoassay (PaGIA, DiaMed-AG, Switzerland). Unfortunately, the results of platelet function tests were not available. However, the diagnosis of HIT was supported by a progressive recovery of baseline platelet values in all patients after the switch from UFH to direct thrombin inhibitors (despite the persistence of other possible causes of thrombocytopenia). Heart transplantation (cardiorenal transplantation in 1 patient) was done between 10 and 20 days after the diagnosis of HIT. At the time of transplantation, all patients had a platelet concentration similar to baseline, although determination of anti-UFH/PF4 antibodies remained positive. None of the patients had thrombotic complications associated with HIT before transplantation. In all patients, the alternative anticoagulant therapy (lepirudin, bivalirudin, or argatroban) was stopped 2 hours before surgery, and UFH alone was used during the CPB period, as is standard practice. Postoperatively, after adequate hemostasis was ensured, the patients were restarted on alternative anticoagulation therapy with fondaparinux or argatroban. No patients showed signs of recurrent HIT. Two patients died. One patient died on day 8 posttransplantation (spontaneous intracerebral hemorrhage) and 1 died on day 27 (fungal sepsis). The other 2 patients are alive at 50 and 24 months after transplantation.

This series is one of the largest studies in patients with ventricular assist devices as a bridge to transplantation and confirms reports of other patients with acute HIT requiring early CPB and UFH.^{3,4} It would be ideal to have access to platelet function tests, using washed platelets, allowing at least confirmation of platelet normalization before transplantation (even if anti-UFH/PF4 antibodies remain detectable). However, these techniques are very complex and are not available in most centers—even in tertiary centers—in Spain.⁵ On this subject, a recent systematic review concluded that the presence of anti-UFH/PF4 antibodies in patients who underwent cardiac surgery was not predictive of thromboembolic complications or postoperative death.⁶

In patients with ventricular assist devices who develop HIT without associated thrombosis, our experience shows that, when platelet function testing is unavailable, early re-exposure to UFH alone during cardiac transplantation and CPB could be an alternative to the use of direct thrombin inhibitors, provided that the preoperative platelet count has recovered and that an alternative anticoagulant treatment is restarted postoperatively.

SUPPLEMENTARY MATERIAL



Supplementary material associated with this article can be found in the online version available at [doi:10.1016/j.rec.2015.02.024](https://doi.org/10.1016/j.rec.2015.02.024).

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