Herein we describe our experience in transplanting 4 highly sensitized patients with a positive prospective crossmatch using a peri-operative desensitization protocol.

The desensitization protocol for highly sensitized patients with positive virtual crossmatch was as follows:

1. Intra-operative PLEx (minimum 3 plasma volume) on cardiopulmonary bypass using albumin as exchange medium with the final exchange utilizing fresh frozen plasma (FFP) replacement.
2. Post-operative PLEx daily for a minimum of 7 days.
3. ATG 3 to 5 mg/kg to be given after PLEx.
4. IVIg 1 g/kg to be given after last PLEx, before patient discharge.
5. Maintenance therapy: (a) mycophenolate mofetil (MMF) 1,000 to 1,500 mg twice daily or mycophenolic acid 1,080 mg twice daily; and prior to the (b) tacrolimus immediate release 0.1 to 0.15 mg/kg/day in 2 divided doses to target a level of 12 to 15 μg/liter; and (c) prednisone 0.5 mg/kg/day.

Results

At the University Health Network, 4 patients underwent peri-operative desensitization as just described (the individual MFI trends for Donor specific antibodies [DSA] for each patient are represented in Figure 1). The baseline characteristics of these patients are summarized in Table 1. All patients were female and blood group O, with mean Class I and Class II PRA levels of 96 and 66%, respectively. The median time on waitlist was 1,011 (range 71 to 1,554) days. None of the patients received desensitization therapies before the peri-operative transplant protocol. In a collaborative effort with the HLA laboratory, a strategy to minimize harm and optimize access was used; this involved the use of selective acceptance of a positive crossmatch while avoiding those antibodies that had higher circulating levels. All patients were in urgent need of cardiac transplantation and the decision was made to accept a positive virtual and actual crossmatch. Flow cytometry crossmatch, HLA antibody single-antigen test and cross-reactive group (CREG) specificity (when available) data are summarized in Table 2. Given the inherent limitations of the test, negative control (NC) values are provided to allow valid comparisons of sera over time.

All 4 patients survived to discharge from hospital and remain alive with a median follow-up of 556 (range 160 to 1,046) days (Table 3). One patient (Patient 1) developed primary graft dysfunction (biopsies done at Days 1 and 6 post-transplant showed no evidence of rejection) requiring mechanical support with veno-arterial extracorporeal membrane oxygenation (VA-ECMO) for 10 days, with subsequent graft function recovery and device explant. Two patients (Patients 2 and 3) developed transient graft dysfunction, which improved within days after transplantation.

At minimum, every patient received 3 mg/kg ATG. The decision to increase ATG dose to 5 mg/kg was dependent on how soon the calcineurin inhibitors were started and how quickly therapeutic levels were achieved.

Only 1 patient (Patient 2) had significant antibody-mediated rejection (pAMR2) 2 weeks post-transplantation, which was treated with PLEx and ATG. Graft function and hemodynamics were normal. Despite receiving a high cumulative ATG dose, the same patient developed cytomegalovirus (CMV) and had 4 episodes of ISHLT Grade 2R cellular rejection requiring pulse corticosteroids and intensification of baseline immunotherapy. This was not surprising given the strongly positive crossmatch. Only 2 patients (Patients 1 and 2) reached the 1-year mark and none developed coronary artery vasculopathy.

In conclusion, we have described a peri-operative desensitization strategy that can be used successfully in selected highly sensitized patients. Although short-term outcomes were positive, long-term outcomes remain less certain, and thus long-term follow-up studies are needed.

Disclosure statement

The authors have no conflicts of interest to disclose.

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Strategy for surgical correction and mitigation of outflow graft twist with a centrifugal-flow left ventricular assist system

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A fully magnetically levitated centrifugal-flow left ventricular assist system (LVAS) has been introduced, with demonstration of improved hemocompatibility and reduced rates of pump malfunction, and stroke.[1–4] This LVAS, the HeartMate 3 (Abbott, Abbott Park, IL) pump, has been observed to have isolated cases of an outflow graft twist occurring in follow-up periods, later in the course of support.[1,5] The mechanism for this development is incompletely understood. It may, however, be related to the proximal outflow graft metallic swivel joint that allows relatively free rotation of this graft once implanted (Figure 1), which is designed to allow initial repositioning during surgery to correct any torque, twist, or kink.

This outflow graft is similar to that of the HeartMate II LVAS (Abbott); however, the abdominal pocket that securely anchors the HeartMate II pump prevents rotation of the outflow graft. The HeartMate 3 pump, in contrast, is implanted intrapericardially or within the thorax and is free to move along with the heart, which makes it prone to positional shifts. Thus, this device can transfer torque to facilitate rotation of the outflow graft in certain physiologic conditions. We assume that helical heart motion (including torsion, tilt, translocation, and base-to-apex contraction) and time-dependent ventricular remodeling may provide the confluence of conditions that could transfer sufficient rotating force to the outflow graft, causing a slow rotation over time leading to mechanical obstruction.

The HeartMate 3 LVAS provides an artificial pulse, and although it could be speculated that this too may play a putative role, it may be less likely. This is because the artificial pulse reaction torque is multiple orders of magnitude lower than that of the native heart and its direction is orthogonal to that which could translate to graft twist.

In this report, we describe two cases that illustrate (1) a framework for detection of this complication, (2) describe a surgical minimally invasive correction technique, and (3) introduce a mechanical mechanism to mitigate against recurrence of twist.

Patient 1: A 41-year-old man with ischemic cardiomyopathy underwent uneventful HeartMate 3 LVAS implant as a bridge to transplant. At 14 months into support, the aortic valve was noted to open with each beat at a speed of 5,100 rpm, and serial radiographs revealed evidence of marked pump migration (Figure 2A). Pump operation was increased to 5,300 rpm, without effect, and a trend to an overall pump flow curve lower than baseline was noted. Lactate dehydrogenase (LDH) levels were not elevated, suggesting absence of pump thrombosis, and he was monitored clinically.

The patient presented with persistent low-flow alarms 4 months after this first presentation, and cardiac ultrasonography revealed decreased inflow and outflow velocities unresponsive to a speed increase up to 5,600 (LDH remained unchanged). A computed tomography-based angiogram demonstrated an outflow graft twist (Figure 2B).

A minimally invasive surgical correction was undertaken under off-pump repair by creating a mini-incision in the sixth intercostal space to expose the base of the outflow graft. The bend relief was cut partially open to expose the underlying twist, which was then untwisted by counter-rotation of the swivel joint in the direction opposite to the twist. Once completed, we anchored the outflow graft swivel joint to prevent rotation by using a specially developed faceted titanium cuff (developed in Berlin as described below in Patient 2 for preventing recurrence).

Patient 2: A 63-year-old man, previously surgically repaired for an outflow graft twist, presented within 3 months with recurrent symptoms and pump flow decrease below 3 liters/min. An angiogram demonstrated retwist close to the pump requiring a second surgical correction. Visual inspection confirmed the diagnosis of an outflow graft twist. The graft was untwisted as it was the first time.

To avoid another recurrence, a customized titanium cuff (Fa. Fittkau Metallbau GmbH, Berlin, Germany) was designed to secure the outflow graft. The graft was rotated back by approximately 90° and locked using the cuff. The cuff consists of 2 hinged parts forming an 8-faceted profile

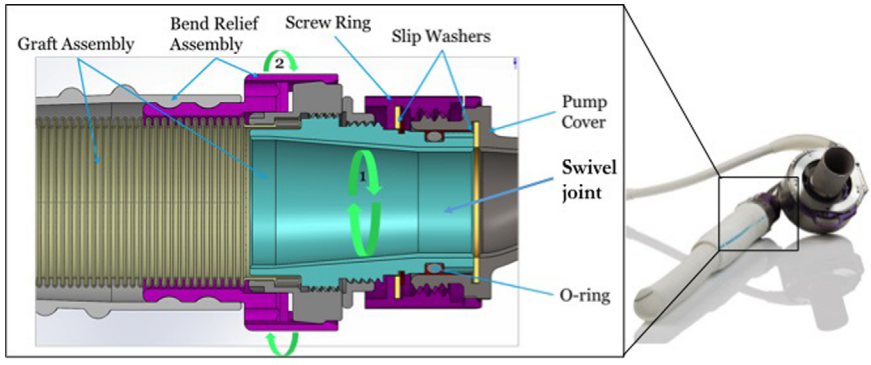

Figure 1 Outflow graft connector mechanism (image obtained courtesy of Abbott, Inc.)