Published in final edited form as:

Hum Immunol. 2009 June ; 70(6): 413–416. doi:10.1016/j.humimm.2009.03.001.

Lack of significant *de novo* HLA allosensitization in ventricular assist device recipients transfused with leukoreduced, ABO identical blood products

Myra Coppage*, Marc Baker, Lawrence Fialkow, Danielle Meehan, Kelly Gettings, Leway Chen, H. Todd Massey, and Neil Blumberg

Department of Pathology and Laboratory Medicine, University of Rochester, Rochester, New York, USA

Abstract

Ventricular assist devices provide support for a failing heart and often serve as a bridge to transplantation. The use of these devices has also been associated with allosensitization to HLA antigens because of transfusion of blood products. Our program established a protocol mandating the use of leukoreduced, irradiated and ABO identical products, including platelets, in patients receiving initial implantations of VAD as a bridge to transplantation. Recipients were tested for anti-HLA antibodies before VAD implantation and monthly postimplantation by cytotoxicity and solid phase assays. We observed minimal *de novo* anti-HLA sensitization (<10%) in this population of 55 patients, each receiving a mean of 90 blood components, using this approach. No patient developed broad sensitization (PRA>50%). In conclusion, The use of leukoreduced, irradiated, ABO identical blood products abrogates broad allosensitization in this highly transfused population.

Keywords

WBC reduction; ABO matching; Allosensitization; PRA

1. Introduction

Ventricular assist devices (VADs) provide mechanical support for a failing heart. Normalization of hemodynamics improves endorgan function, with approximately 70% of patients surviving until cardiac transplantation [1]. VADs provide a bridge to cardiac transplantation and may also be used as long-term “destination” therapy for patients who are not candidates for transplantation. Several VAD devices are available (*e.g.*, HeartMate, Novacor, Thoratec); these devices are composed of metal, polymers and porcine tissue. The pumps are primarily designed to support the left ventricle, but some devices may also assist the right [2]. The implantation of certain assist devices has been associated with many systemic irregularities including defects in coagulation and fibrinolysis cascades, infections (bacterial and fungal), decreased and TH-2 skewed T-cell responses, increased B-cell numbers and production of IgG, and higher serum levels of inflammatory molecules [3-6]. Implantation has also been associated with allosensitization to HLA antigens, presumably due to transfused blood products [7-10], although some reports have suggested alternative mechanisms [11-13]. Allosensitization may greatly increase the wait time for a compatible

graft, and the odds of an antibody-mediated rejection episode after transplantation. Evidence from randomized trials in patients with leukemia suggests that use of leukoreduced blood components and ABO identical platelets reduces the likelihood of HLA allosensitization [14]. Many transfusion services employ leukoreduced transfusions, but few attempt to give only ABO identical platelet transfusions. Based on longstanding evidence at our institution [15-17], we used a protocol mandating the use of leukoreduced, irradiated, and ABO identical products, including platelets, in patients receiving initial implantations of VAD as a bridge to transplantation. Cellular products were also gamma irradiated. We observed minimal *de novo* anti-HLA sensitization in this population using this approach.

2. Subjects and methods

2.1. Patients

Between September 2001 and August 2007, 55 patients were implanted with a VAD as a bridge to transplantation and were followed by the HLA laboratory. Demographic characteristics are summarized in Table 1. All blood products were leukoreduced and irradiated and were ABO identical except for FFP, which were ABO identical but not manipulated. Heart transplantation was achieved for 37 (67%) VAD recipients; eight patients died without transplantation at a mean of 215 days (range, 13–630 days). Ten patients remain on the waitlist with a VAD in place.

2.2. Human subjects protection

The Research Subjects Review Board at the University of Rochester Medical Center approved this study. Research data was coded such that subjects could not be identified, directly or through linked identifiers, in compliance with the Department of Health and Human Services Regulations for the Protection of Human Subjects (45 CFR 46.10 {b} (4)).

2.3. Panel reactive antibody analysis and crossmatch

Anti-HLA antibody assessment was initially performed within 2 weeks before VAD placement and at least monthly until the recipient underwent transplantation or was deemed not to be a candidate for transplantation. Sera used in complement dependent cytotoxicity (CDC) assays were heat treated to reduce IgM antibodies. CDC panel reactive antibodies (PRA) were determined by reactivity to a cell panel (GenTrak, Inc., Liberty, NC) of 30 HLA-typed donors comprising well-defined HLA specificities. Further testing was performed using an enzyme-linked immunoabsorbent assay (ELISA; GTI, Inc., Waukesha, WI) in which wells contained either pooled HLA antigen or antigen from specific donors for specific antibody identification and/or a Luminex (LM) assay (Tepnel, Stamford CT) in which HLA antigen (pooled, specific donor or recombinant) was bound to fluorescent bead particles and assayed in a flow based method. Donor specific crossmatching was performed within 24 hours of transplantation by CDC and, in most cases, flow cytometry using serum drawn immediately before transplant.

3. Results

3.1. Panel reactive antibodies

Four patients (one female and three male) demonstrated anti-HLA specific antibodies by CDC and ELISA before and after VAD placement. Of the remaining 51 previously unsensitized patients, 5 (10%) developed *de novo* PRA as detected by the CDC or Luminex (LM) method after VAD placement (Fig. 1). Of these five, two were female and the three were male; two received Heartmate II, two received Heartmate XVE, and one received a Thoratec. Table 2 details the sensitization of these five patients. Four recipients in this group underwent transplantation at 6 weeks, 2 months, and 2 at 4 months. One VAD recipient died

on the waitlist at 20 months. There was no correlation between existence or development of anti-HLA antibody and amount of blood products received ($p = 0.7$). We did observe a steady increase in patients demonstrating reactivity in ELISA over time. The activity of these sera was also seen in wells that did not contain HLA antigen, indicating false-positive results consistent with observations of other groups [12]. False-positive results were observed in both the screening and identification assays with OD readings in the no antigen well >0.5 . In 2006, the laboratory validated the LM solid phase assay for use in the VAD population as, in our hands, it does not demonstrate the rate of false positive results. Where available, sera from patients that had been tested in ELISA were also tested by LM screening beads.

3.2. Crossmatching

All CDC crossmatches were negative at time of transplantation. Of the patients, 60% were reactive in the flow cytometric crossmatch. The presence of reactivity in the B-cell or T- and B-cell flow crossmatches was not a predictor of patient or graft survival, as no statistically significant differences were observed between the groups using Kaplan-Meier analysis by either the log rank or Wil-coxin tests (data not shown). However, there was a significant correlation between a false-positive ELISA result and positive flow crossmatch ($p < 0.05$), suggesting that the nonspecific antibody reactions in the ELISA were also observed in the flow crossmatch, especially with B cells. Pronase, a proteolytic enzyme that cleaves the Fc receptor and may decrease the incidence of false positive B-cell crossmatches [18], was not in use during the period under study.

3.3. Patient and graft survival

There was no correlation between patients who had or developed anti-HLA antibody and survival ($p = 0.4$). However, a significant correlation exists between survival and use of blood products ($p < 0.0001$). The 20 deceased patients received an average of 124 (± 18) combined blood products, whereas the 34 surviving patients received 61 (± 27).

4. Discussion

The evidence for HLA allosensitization associated with ventricular assist devices remains controversial. We report a series spanning 7 years of VAD implantation as a bridge to transplantation. As part of routine immune monitoring, CDC testing for anti-HLA antibodies was performed. In contrast to what many centers have reported, we observed minimal development of these antibodies as a result of immune activation to the VAD or the administration of large numbers of blood products. Others [19,20] have observed decreased sensitization when using the Novacor (WorldHeart, Ottawa, ON, Canada) or DeBakey Axial (Micromed Technology, Houston, TX) or HeartMate II (Thoratec, Pleasanton, CA) [21] devices, and increased risk of sensitization for recipients of the Heart-Mate I (Thoratec, Pleasanton, CA) [8,22]. We observed no correlation between sensitization and the type of device. Multiparous women were the only subjects at increased risk for allosensitization, as three of the eight women in the population had or developed anti-HLA antibody. Overall, however, our results indicate minimal allosensitization, and suggest that center-specific transfusion practices should be considered and reported when comparing single center studies of allosensitization with VAD devices.

Serum from VAD patients does exhibit reactivity in ELISA assays, but reactivity occurs even in wells that do not contain HLA antigen. These are clearly false positive reactions. Newell *et al.* [12] reported that IgG antibodies detected in the ELISA assay of serum from VAD patients were anti-albumin antibodies, a reagent commonly used in ELISA assays. The positive reactions converted to negative when sera were pre-incubated with albumin-coated

beads. Our data indicate a similar phenomenon; however, when Luminex technology for antibody testing was implemented, false-positive reactions were not observed. LM microparticles are coated with HLA antigen from a pool of donors (screening), single donors (identification), or recombinant HLA protein (epitope identification). Although the buffers used in the assays with these beads does contain albumin, we do not observe the false-positive reactions seen in ELISA. In our hands, the Luminex beads provide increased sensitivity without a decrease in specificity. In fact, cytotoxic PRA testing is now rarely performed for cardiac recipients.

Many investigators have been interested in the ability of blood transfusions to immunomodulate allosensitization [23-28]. Our group has reported that the use of leukoreduced transfusions is associated with a decrease in RBC immunization [16]. We have also observed that transfusion of ABO-mismatched platelets is associated with increased morbidity and mortality in patients undergoing induction therapy for hematopoietic stem cell transplant for acute leukemia [15,29,30] and with unfavorable outcomes among cardiac surgery patients [17]. Others [31] have observed that leukocyte depletion of platelets prevents HLA alloimmunization. Based on these observations the policy mandating the use of leukoreduced and ABO identical products, including platelets was applied for patients receiving initial implantations of VAD as a bridge to transplantation.

Although the lack of a control group of patients who received unmodified blood is a limitation to our study, historic literature provides evidence for allosensitization using unmodified blood. Table 3 is a summary of reported allosensitization among VAD recipients (where $n > 20$) reported from several centers over the last two decades. A trend toward decreasing allosensitization is apparent with the increasing use of leukoreduction. Leukoreduction became standard practice at most large centers in the late 1990s, and studies that include more patients after the year 2000, report lower rates of allosensitization. Only Moazami *et al.* [7] separated data from patients who received only leukoreduced products from those who did not. Of seven recipients who received only leukoreduced products, only one (14%) developed a PRA greater than 10% whereas more than 50% of the 33 patients receiving non-leukoreduced transfusions developed anti-HLA antibody with PRA greater than 10%.

We have observed that soluble immune modulatory factors (sCD40L, IL-8, and RANTES) are present and biologically active in platelet concentrates [32-34] and non-leukoreduced red cells, and to a lesser extent this may be true of FFP as well. Our working hypothesis is that intravenously administered blood components (including FFP), administered as a bolus (as opposed to being produced in a paracrine manner) access the lymphatic system where immune effectors reside, and modulate their responses. Several groups have previously reported systemic alterations and immune dysregulation involving B cells after VAD implantation [3,35,36]. Before the general acceptance of universal leukoreduction, a prime indication of this effect on B-cell immunity was the production of anti-HLA antibodies. MHC molecules are immunogenic and provide a stimulus for an antibody response. For this reason, anti-HLA responses became a focus of discussion regarding the hazards of blood transfusion in VAD patients, and “masked” the general immune dysregulation. We believe that the immunomodulatory factors present in blood transfusion, especially those that contain white cells or platelets, contribute to a systemic TH2 response, including nonspecific activation of B cells and upregulation of immunoglobulin production [4]. This response may include specific (*e.g.*, anti-albumin), nonspecific (*e.g.*, natural anti-ABO), and memory (*e.g.*, anti-HLA from pregnancy) antibody responses. Our group has also reported the formation of circulating immune complexes of ABO antigen and their corresponding antibodies in patients who received ABO unmatched platelets [37,38]. We believe that any or all of these phenomena may interfere with immune assays, especially those that use an anti-

immunoglobulin (second-step) reagent such as ELISA, and flow or AHG crossmatch. For the population in this study, clinical decisions regarding cardiac transplantation of VAD recipients were based in the cytotoxicity crossmatch and antibody panel. Recently, however, the LM antibody identification test has proved to be both sensitive and specific, although, like other solid-phase assays, LM uses an anti-human immunoglobulin secondary step. It is possible that the particulate nature of the beads precludes weak, nonspecific reactions.

In summary, although the data are retrospective and not randomized or internally controlled, our exclusive use of leukoreduced, irradiated, and ABO-identical blood transfusions almost completely abrogated specific, cytotoxic anti-HLA allosensitization in a heavily transfused group of 55 patients implanted with VADS, including a majority who underwent cardiac allotransplantation. Because of the immunomodulatory potential of material transfused to these recipients, we believe that our protocol minimizes immune costimulation, inflammation, and antigenic stimulation for antibody sensitization. Our results are of interest because they confirm that use of leukoreduced, ABO identical, irradiated blood components have low allosensitization potential in patients thought to be immunologically intact. There has been speculation that such modification would not prevent allosensitization except in patients undergoing immunosuppressive or myeloablative chemotherapy. Our results demonstrate this not to be the case, at least when ABO matching and irradiation are also part of the transfusion protocol.

References

- [1]. Kirklin JK, Holman WL. Mechanical circulatory support therapy as a bridge to transplant or recovery (new advances). *Curr Opin Cardiol*. 2006; 21:120. [PubMed: 16470148]
- [2]. Marcel R, Meyer DM. An overview of approved and investigational left ventricular assist devices. *Proc Bayl Univ Med Cent*. 2004; 17:407. [PubMed: 16200128]
- [3]. Hampton CR, Verrier ED. Systemic consequences of ventricular assist devices: Alterations of coagulation, immune function, inflammation, and the neuroendocrine system. *Artif Organs*. 2002; 26:902. [PubMed: 12406140]
- [4]. Rothenburger M, Wilhelm M, Hammel D, Schmid C, Plenz G, Tjan TDT, Baba H, et al. Immune response in the early postoperative period after implantation of a left-ventricular assist device system. *Transplant Proc*. 2001; 33:1955. [PubMed: 11267586]
- [5]. Ankersmit HJ, Edwards NM, Schuster M, John R, Kocher A, Rose EA, et al. Quantitative changes in T-cell populations after left ventricular assist device implantation: Relationship to T-cell apoptosis and soluble CD95. *Circulation*. 1999; 100(19 Suppl):II211. [PubMed: 10567306]
- [6]. Itescu S, Schuster M, Burke E, Ankersmit J, Kocher A, Deng M, et al. Immunobiologic consequences of assist devices. *Cardiol Clin*. 2003; 21:119. [PubMed: 12790051]
- [7]. Moazami N, Itescu S, Williams MR, Argenziano M, Weinberg A, Oz MC. Platelet transfusions are associated with the development of anti-major histocompatibility complex class I antibodies in patients with left ventricular assist support. *J Heart Lung Transplant*. 1998; 17:876. [PubMed: 9773859]
- [8]. Massad MG, Cook DJ, Schmitt SK, Smedira NG, McCarthy JF, Vargo RL, McCarthy PM. Factors influencing HLA sensitization in implantable LVAD recipients. *Ann Thorac Surg*. 1997; 64:1120. [PubMed: 9354538]
- [9]. Karpinski M, Pochinco D, Dembinski I, Laidlaw W, Zacharias J, Nickerson P. Leukocyte reduction of red blood cell transfusions does not decrease allosensitization rates in potential kidney transplant candidates. *J Am Soc Nephrol*. 2004; 15:818. [PubMed: 14978185]
- [10]. Gonzalez-Stawinski GV, Atik FA, McCarthy PM, Roselli EE, Hoercher K, Navia JL, et al. Early and late rejection and HLA sensitization at the time of heart transplantation in patients bridged with left ventricular assist devices. *Transplant Proc*. 2005; 37:1349. [PubMed: 15848717]
- [11]. Kerman RH, Radovancevic B, Przybylowski P, Frazier OH, Thomas C, Kahan BD. LVAD treated heart recipients do not have deleterious HLA antibody. *J Heart Lung Transplant*. 2001; 20:211. [PubMed: 11250384]

- [12]. Newell H, Smith JD, Rogers P, Birks E, Danskine AJ, Fawson RE, Rose ML. Sensitization following LVAD implantation using leucodepleted blood is not due to HLA antibodies. *Am J Transplant*. 2006; 6:1712. [PubMed: 16827875]
- [13]. Pamboukian SV, Costanzo MR, Dunlap S, Rayburn B, Westfall AO, You ZY, et al. Relationship between bridging with ventricular assist device on rejection after heart transplantation. *J Heart Lung Transplant*. 2005; 24:310. [PubMed: 15737758]
- [14]. Trial to Reduce Alloimmunization to Platelets Study Group. Leukocyte reduction and ultraviolet B irradiation of platelets to prevent alloimmunization and refractoriness to platelet transfusions. *N Engl J Med*. 1997; 337:1861. [PubMed: 9417523]
- [15]. Blumberg N, Heal JM, Kirkley SA, DiPersio JF, Rapoport AP, Rowe JM. Leukodepleted-ABO-identical blood components in the treatment of hematologic malignancies: A cost analysis. *Am J Hematol*. 1995; 48:108. [PubMed: 7847323]
- [16]. Blumberg N, Heal JM, Gettings KF. WBC reduction of RBC transfusions is associated with a decreased incidence of RBC alloimmunization. *Transfusion*. 2003; 43:945. [PubMed: 12823755]
- [17]. Blumberg N, Heal JM, Hicks GL Jr, Risher WH. Association of ABO-mismatched platelet transfusions with morbidity and mortality in cardiac surgery. *Transfusion*. 2001; 41:790. [PubMed: 11399821]
- [18]. Vaidya S, Cooper TY, Avandsalehi J, Barnes T, Brooks K, Hymel P, et al. Improved flow cytometric detection of HLA alloantibodies using pronase: Potential implications in renal transplantation. *Transplantation*. 2001; 71:422. [PubMed: 11233905]
- [19]. Grinda JM, Bricourt MO, Amrein C, Salvi S, Guillemain R, Francois A, et al. Human leukocyte antigen sensitization in ventricular assist device recipients: A lesser risk with the DeBakey axial pump. *Ann Thorac Surg*. 2005; 80:945. [PubMed: 16122460]
- [20]. Baran DA, Gass AL, Galin ID, Zucker MJ, Arroyo LH, Goldstein DJ, et al. Lack of sensitization and equivalent post-transplant outcomes with the Novacor left ventricular assist device. *J Heart Lung Transplant*. 2005; 24:1886. [PubMed: 16297796]
- [21]. George I, Colley P, Russo MJ, Martens TP, Burke E, Oz MC, et al. Association of device surface and biomaterials with immunologic sensitization after mechanical support. *J Thorac Cardiovasc Surg*. 2008; 135:1372. [PubMed: 18544389]
- [22]. Pagani FD, Dyke DB, Wright S, Cody R, Aaronson KD. Development of anti-major histocompatibility complex class I or II antibodies following left ventricular assist device implantation: Effects on subsequent allograft rejection and survival. *J Heart Lung Transplant*. 2001; 20:646. [PubMed: 11404170]
- [23]. Rossini AA, Mordes JP, Greiner DL, Nakano K, Appel MC, Handler ES. Spleen cell transfusion in the Bio-Breeding/Worcester rat. Prevention of diabetes, major histocompatibility complex restriction, and long-term persistence of transfused cells. *J Clin Invest*. 1986; 77:1399. [PubMed: 3958191]
- [24]. Blumberg N, Heal JM. Blood transfusion immunomodulation: The silent epidemic. *Arch Pathol Lab Med*. 1998; 122:117. [PubMed: 9499352]
- [25]. Blumberg N. Deleterious clinical effects of transfusion immunomodulation: Proven beyond a reasonable doubt. *Transfusion*. 2005; 45(2 Suppl):33S. [PubMed: 16086785]
- [26]. Oh JH, McClure HM, Galvao MM. Comparison of immunogenicity of fresh and stored blood. A study in rhesus monkeys. *Transplantation*. 1982; 33:198. [PubMed: 7036473]
- [27]. Claas FH, Roelen DL, van Rood JJ, Brand A. Modulation of the alloimmune response by blood transfusions. *Transfus Clin Biol*. 2001; 8:315. [PubMed: 11499985]
- [28]. Blajchman MA, Dzik S, Vamvakas EC, Sweeney J, Snyder EL. Clinical and molecular basis of transfusion-induced immunomodulation: Summary of the proceedings of a state-of-the-art conference. *Transfus Med Rev*. 2001; 15:108. [PubMed: 11309732]
- [29]. Goldman J, Liesveld J, Nichols D, Heal J, Blumberg N. ABO incompatibility between donor and recipient and clinical outcomes in allogeneic stem cell transplantation. *Leuk Res*. 2003; 27:489. [PubMed: 12648507]
- [30]. Heal JM, Kenmotsu N, Rowe JM, Blumberg N. A possible survival advantage in adults with acute leukemia receiving ABO-identical platelet transfusions. *Am J Hematol*. 1994; 45:189. [PubMed: 8141126]

- [31]. van Marwijk Kooy M, van Prooijen HC, Moes M, Bosma-Stants I, Akkerman JW. Use of leukocyte-depleted platelet concentrates for the prevention of refractoriness and primary HLA alloimmunization: A prospective, randomized trial. *Blood*. 1991; 77:201. [PubMed: 1984797]
- [32]. Blumberg N, Gettings KF, Turner C, Heal JM, Phipps RP. An association of soluble CD40 ligand (CD154) with adverse reactions to platelet transfusions. *Transfusion*. 2006; 46:1813. [PubMed: 17002639]
- [33]. Kaufman J, Spinelli SL, Schultz E, Blumberg N, Phipps RP. Release of biologically active CD154 during collection and storage of platelet concentrates prepared for transfusion. *J Thromb Haemost*. 2007; 5:788. [PubMed: 17403203]
- [34]. Khan SY, Kelher MR, Heal JM, Blumberg N, Boshkov LK, Phipps R, et al. Soluble CD40 ligand accumulates in stored blood components, primes neutrophils through CD40, and is a potential cofactor in the development of transfusion-related acute lung injury. *Blood*. 2006; 108:2455. [PubMed: 16772606]
- [35]. Rothenburger M, Wilhelm M, Hammel D, Schmid C, Plenz G, Tjan TD, et al. Immune response in the early postoperative period after implantation of a left-ventricular assist device system. *Transplant Proc*. 2001; 33:1955. [PubMed: 11267586]
- [36]. Itescu S, John R. Interactions between the recipient immune system and the left ventricular assist device surface: Immunological and clinical implications. *Ann Thorac Surg*. 2003; 75(6 Suppl):S58. [PubMed: 12820736]
- [37]. Heal JM, Masel D, Blumberg N. Interaction of platelet fc and complement receptors with circulating immune complexes involving the ABO system. *Vox Sang*. 1996; 71:205. [PubMed: 8958643]
- [38]. Heal JM, Masel D, Rowe JM, Blumberg N. Circulating immune complexes involving the ABO system after platelet transfusion. *Br J Haematol*. 1993; 85:566. [PubMed: 8136280]

Fig 1.

Four recipients demonstrated alloantibody detected in the pre-VAD sample. Five patients developed a PRA greater than 5% detected by CDC or LM at any time after VAD placement, one only in the pretransplant sample. The number of observations in each category is indicated above the bar.

Table 1

Demographic characteristics of VAD recipients

Characteristic	n
Gender	
Male	47
Female	8
Age, years, mean (range)	53 (19–73)
Etiology	
Ischemic	39
Nonischemic	16
Device	
Thoratec	18
HeartMate XVE	14
HeartMate II	13
ABIOMED	6
Levitronix Centrimag	2
Dual devices	2 ^a
Blood products, mean (SD)	
RBC	51 (32)
Platelets	7 (6)
FFP	24 (18)
Cryoprecipitate	2 (2)

^aOne patient had Heartmate LVAD and ABIOMed RVAD implants; the second had Heartmate II and Thoratec paracorporeal pump.

Table 2

Specific sensitization and donor crossmatching for the five recipients who developed de novo anti-HLA antibody after VAD implantation

Patient no.	Gender	Device	Sensitization history	Crossmatch/transplant
1	Male	HeartMate II	7% CDC, 23% LM with anti-B7, B40, B8 specificities	Transplanted with B7, B40, B8-negative donor; FACS T and B+
2	Male	HeartMate II	30 days 30% CDC, 46% LM with anti-A2,A28	Deceased at 20 months with VAD
3	Male	HeartMate XVE	30 days 17% CDC weak anti-HLA-B7,53% ELISA B7C	Transplanted with HLA-B7–negative donor; FACS compatible
4	Female	Thoratec BiVAD	30 days 7% CDC/28% ELISA anti-HLA-A1	Transplanted with HLA-A1 negative donor, B-cell FACS+
5	Female	HeartMate XVE	60 days LM B7, 27, 60; 120 days CDC 6% B7	Transplanted with antibody-negative donor; FACS weak B+; dead at 16 months

Table 3

Literature review of allosensitization associated with VAD

Study authors, year	Study period	Center	VAD patients (n)	% Sensitized	Blood modification
Massad et al., 1997	1992–1995	Cleveland	53	65%	Few leukoreduced
Moazami et al., 1998	1990–1996	Columbia	40	<50%	7/40 Filtered
Pagani et al., 2000	1996–2000	Michigan	38	28%	Most leukoreduced
McKenna et al., 2002	1995–2000	Minneapolis	29	28%	Few leukoreduced
John et al., 2003	1992–1999	Columbia	105	66%	Not reported
Kumpati et al., 2004	1991–2000	Cleveland	231	<5%	Leukoreduced after 1995
Drakos et al., 2006	1993–2003	Utah	51	33%	Most leukoreduced
Drakos et al., 2007	1993–2002	Utah	71(54/17)	35% vs. 58%	Leukoreduced vs FFP
George et al., 2008	1999–2006	Columbia	60 (36/24)	28% vs. 8%	All leukoreduced