

5. Heart transplantation

5.1. Induction therapy

Cantarovich, M. et al. (2004). Antithymocyte globulin induction allows a prolonged delay in the initiation of cyclosporine in heart transplant patients with postoperative renal dysfunction. *Transplantation*, 78, 779-781. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/15371689>

- Patients experiencing post-operative renal dysfunction received rATG induction with delayed initiation of cyclosporine. Compared to controls that received cyclosporine beginning on POD2, no significant differences in acute rejection or patient survival were observed.

Carrier, M. et al. (2007). Basiliximab and rabbit anti-thymocyte globulin for prophylaxis of acute rejection after heart transplantation: a non-inferiority trial. *Journal of Heart and Lung Transplantation*, 26, 258-263.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17346628>

- Patients receiving rATG induction experienced less acute rejection at six months than those receiving basiliximab. Non-inferiority of basiliximab was not demonstrated in this investigation.

Goland, S. et al. (2008). Induction Therapy with Thymoglobulin After Heart Transplantation: Impact of Therapy Duration on Lymphocyte Depletion and Recovery, Rejection, and Cytomegalovirus Infection Rates. *Journal of Heart and Lung Transplantation*, 27, 1115-1121.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/18926403>

- rATG induction consisting of 1.5 mg/kg doses given for five days was compared to a seven day course. Patients receiving the longer induction regimen experienced significantly less acute rejection ($\geq 1B$) at one year without an increase in CMV or bacterial infections.

Lindenfeld, J. et al (2004). Drug Therapy in the Heart Transplant Recipient Part I: Cardiac Rejection and Immunosuppressive Drugs. *Circulation*, 110, 3734-3740.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15596559>

- First article in a four-part series reviewing medication management for heart transplant recipients. This one focuses on rejection and induction agents.

Mattei, M. F. et al. (2007). Lower risk of infectious deaths in cardiac transplant patients receiving basiliximab versus anti-thymocyte globulin as induction therapy. *Journal of Heart and Lung Transplantation*, 26, 693-699. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/17613399>

- Prospective, randomized, multi-center comparison of basiliximab and rATG. The incidences of the composite safety end-point (serum sickness, fever, cutaneous rash, anaphylaxis, infection, thrombocytopenia, leukopenia and PTLS) and death due to infection were significantly less in the basiliximab

group. No differences in the composite efficacy endpoint (death, graft loss, acute rejection > 1B, acute rejection associated with hemodynamic compromise or treated with antibody therapy, loss to follow up) were observed.

Penninga L, Møller CH, Gustafsson F, Gluud C, Steinbrüchel DA. (2013). Immunosuppressive T-cell antibody induction for heart transplant recipients. Cochrane Database Systematic Reviews.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/24297433>

- This review included 22 RCTs evaluating the use of antibody induction for heart transplant recipients. Acute rejection occurred less frequently with IL2-RA compared to no induction as well as with polyclonal antibody induction compared to IL2-RA and no significant differences regarding mortality, infection, or CAV, cancer or adverse events were detected. However, all included studies were thought to have a high risk of bias and no clear indication of benefit or harm associated with antibody induction could be demonstrated by this review.

5.2. Maintenance therapy

Eisen, H. J. et al. (2003). Everolimus for the Prevention of Allograft Rejection and Vasculopathy in Cardiac-Transplant Recipients. *New England Journal of Medicine*, 349, 847-858.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12944570>

- Randomized, double-blind comparison of 1.5 and 3 mg of everolimus and azathioprine in combination with cyclosporine and steroids. Patients receiving either everolimus dose experienced significantly less vasculopathy, composite efficacy endpoint (death, graft loss or retransplantation, loss to follow-up, biopsy-proven acute rejection of grade 3A, or rejection with hemodynamic compromise) and CMV infection.

Eisen, H. J. et al. (2005). Three-Year Results of a Randomized, Double-Blind, Controlled Trial of Mycophenolate Mofetil Versus Azathioprine in Cardiac Transplant Recipients. *Journal of Heart and Lung Transplantation*, 24, 517-525. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/15896747>

- Patients receiving AZA were retransplanted or died more frequently and had a shorter time to retransplantation or death than the MMF group. MMF-treated patients also had a smaller change in mean maximal intimal thickness compared to AZA (P = 0.056).

Eisen, H. J. et al. (2013). Everolimus Versus Mycophenolate Mofetil in Heart Transplantation: A Randomized, Multicenter Trial. *American Journal of Transplantation*, 13, 1203-1216.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23433101>

- Everolimus 1.5 mg and 3 mg daily plus steroids and cyclosporine targeting reduced trough concentration were compared to MMF plus steroids and traditional cyclosporine dosing with and without induction therapy. Patients receiving 3 mg of everolimus daily experienced increased mortality and this regimen was terminated. Everolimus was non-inferior to MMF with respect to the primary composite efficacy endpoint (biopsy-proven acute rejection, acute rejection associated with hemodynamic compromise, graft loss/retransplant, death or loss to follow-up) at 12 and 24 months. Mortality, primarily related to infection, at month 3 was higher when everolimus was combined with rATG induction, but was similar at 24 months.

Fang, J. C. et al. (2002). Effect of vitamins C and E on progression of transplant-associated arteriosclerosis: a randomised trial. *Lancet*, 359, 1108–1113. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11943259>

- Prospective, double-blind study comparing vitamin A and E supplementation (n = 19) to placebo (n = 21). Patients receiving supplementation did not experience significant change in intimal index compared to those receiving placebo.

Fuchs, U. et al. (2012). Efficacy and Safety of Low-Dose Everolimus as Maintenance Immunosuppression in Cardiac Transplant Recipients. *Journal of Transplantation*, 2012, Article ID 976921.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22577516>

- Everolimus 0.75 mg BID targeting trough levels of 5-8 mcg/L was compared to 0.5 mg BID targeting levels of 3-5 mcg/L and no significant difference with respect to the primary composite endpoint including death, rejection, and discontinuation of everolimus was detected.

Grimm, M. et al. (2006). Superior prevention of acute rejection by tacrolimus vs. cyclosporine in heart transplant recipients--a large European trial. *American Journal of Transplantation*, 6, 1387-1397.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16686762>

- Incidence of BPAR \geq 1B and 3A at six months was significantly decreased for patients receiving tacrolimus compared to cyclosporine. TAC-treated patients also developed significantly more NODAT, but less hyperlipidemia and HTN.

Guethoff, S. et al. (2013). Ten-year results of a randomized trial comparing tacrolimus versus cyclosporine a in combination with mycophenolate mofetil after heart transplantation. *Transplantation*, 95, 629-634.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23423270>

- Freedom from acute rejection was significantly greater at 1, 5 and 10 years for patients receiving tacrolimus-based maintenance immunosuppression. Freedom from CAV was also increased for the tacrolimus group compared to

those receiving cyclosporine. No significant differences in patient survival at 1, 5, or 10 years were observed.

Kobashigawa, J. et al. (1998). A randomized active-controlled trial of mycophenolate mofetil in heart transplant recipients. *Transplantation*, 66, 507-515. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9734496>

- Rejection that required treatment as well as mortality at one year were significantly reduced in the MMF group. MMF-treated patients did experience more opportunistic infections, predominately HSV.

Kobashigawa, J and B. M. Meiser. (2005). Review of Major Clinical Trials with Mycophenolate Mofetil in Cardiac Transplantation. *Transplantation*, 80, S235-S243. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16251856>

- Review summarizing MMF efficacy studies as well as use in pediatric heart transplantation, coronary allograft vasculopathy and therapeutic drug monitoring.

Kobashigawa, J. A. (2006). Tacrolimus with mycophenolate mofetil (MMF) or sirolimus vs. cyclosporine with MMF in cardiac transplant patients: 1-year report. *American Journal of Transplantation*, 6, 1377-1386.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16686761>

- No significant difference in the primary endpoint of grade 3A or greater rejection of rejection associated with hemodynamic compromise was detected. However, significant differences in any treated rejection, median serum creatinine and triglycerides occurred and favored the combination of tacrolimus and MMF.

Lindenfeld, J. et al. (2004). Drug Therapy in the Heart Transplant Recipient Part II: Immunosuppressive Drugs. *Circulation*, 110, 3858-3865. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15611389>

Lindenfeld, J et al. (2005). Drug Therapy in the Heart Transplant Recipient Part III: Common Medical Problems. *Circulation*, 111-117. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15630040>

Page, R. L. et al. (2005). Drug Therapy in the Heart Transplant Recipient Part IV: Drug-Drug Interactions. *Circulation*, 111, 230-239. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15657387>

- These three complete the four-part series reviewing medication management for heart transplant recipients. Maintenance immunosuppression, drug-drug interactions and a variety of common post-transplant disease states including hypertension, hyperlipidemia, coronary allograft vasculopathy, osteoporosis,

diabetes and depression are discussed. The series is a bit dated, but provides a nice introduction for students and residents.

Patel, J. K. and J. A. Kobashigawa. (2007). Tacrolimus in heart transplant recipients: An overview. *Biodrugs*, 21, 139-143. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17516709>

- Review of investigations comparing tacrolimus to cyclosporine for cardiac transplantation.

Topilsky, Y. (2012). Sirolimus as Primary Immunosuppression Attenuates Allograft Vasculopathy with Improved Late Survival and Decreased Cardiac Events After Cardiac Transplantation. *Circulation*, 125, 708-720. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22207715>

- Retrospective evaluation of converting CNI to sirolimus-based maintenance immunosuppression. Plaque index progression, vascular remodeling, freedom for cardiac events and patient survival were all improved with conversion to sirolimus.

5.3. Desensitization therapy

Morrow, WR et al. (2012). Rapid Reduction in Donor-Specific Anti-Human Leukocyte Antigen Antibodies and Reversal of Antibody-Mediated Rejection With Bortezomib in Pediatric Heart Transplant Patients. *Transplantation*, 93, 319–324. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22179403>

- This article documents the first use of bortezomib for cardiac transplant recipients in four pediatric heart recipients with biopsy-proven AMR, hemodynamic compromise, positive crossmatch, and high titer class I DSA.

Patel, J et al. (2011). Reduction of alloantibodies via proteasome inhibition in cardiac transplantation. *J Heart Lung Transplant*, 30, 1320 – 6. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/21968130>

- The first clinical experience using a plasma-cell-depleting strategy with bortezomib to reduce anti-HLA antibodies in the heart transplant population.

Kobashigawa, JA et al. (2011). The long-term outcome of treated sensitized patients who undergo heart transplantation. *Clin Transplant*, 25, E61–E67. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/20973825>

- This study was done to determine whether reduction in circulating antibodies pre-transplant with plasmapheresis, intravenous gamma globulin and rituximab improves post-transplant outcomes.

Zeevi, A et al. (2012). HLA antibody profiling in thoracic transplantation undergoing desensitization therapy. *Curr Opin Organ Transplant*, 17, 416–422. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22790076>

- This article reviews HLA antibody profiling pre-transplant and the effect of desensitization protocols on post-transplant outcomes.

Urban, M et al. (2012.) Alloimmunosenitization in Left Ventricular Assist Device Recipients and Impact on Posttransplantation Outcome. *ASAIO Journal*, 58, 554–561.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23069898>

- This article presents the current state of knowledge of possible immunologic mechanisms involved in alloimmunization of LVAD recipients, outlines new methods of antibody detection, compares various desensitization strategies, and presents an overview of clinical data assessing the impact of sensitization on posttransplantation outcome.

Chang, D et al. (2012). The use of the calculated panel reactive antibody and virtual crossmatch in heart transplantation. *Curr Opin Organ Transplant*, 17, 423–426. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22790077>

- This article reviews the use of calculated panel reactive antibody and virtual crossmatch in heart transplant as well as current desensitization strategies.

Picascia, A et al. (2012). Current Concepts in Histocompatibility During Heart Transplant. *Experimental and Clinical Transplantation*, 3, 209-218. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/22631055>

- This article reviews strategies for detection of antibodies and current strategies for desensitization pre-transplant.

Eckman, PM et al. (2010). Immunosuppression in the sensitized heart transplant recipient. *Current Opinion in Organ Transplantation*, 15, 650–656. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/20689437>

- This article reviews contemporary approaches to desensitization prior to and immunosuppression following heart transplant.

5.4. Management of rejection

Nair, N et al. (2011). Current and future challenges in therapy for antibody-mediated rejection. *J Heart Lung Transplant*, 30, 612–7. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/21474341>

- This article discusses the challenges in treating antibody mediated rejection and provides a critical analysis of current and possible future therapies.

Aggarwal, A et al. (2012). Low-Dose Rituximab Therapy for Antibody-Mediated Rejection in a Highly Sensitized Heart-Transplant Recipient. *Tex Heart Inst J*, 39(6):901-5. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/23304051>

- This is a case report regarding the role of low-dose rituximab as therapy for antibody-mediated rejection in heart-transplant patients.

Imamura, T et al. (2013). Successful Treatment of Hemodynamic Compromise Caused by Antibody-Mediated and Cellular Rejection in a Recipient 12 years After Heart Transplantation. *Int Heart J*, 54, 328-331. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/24097224>

- This is a case report of successful treatment of rejection with repeated plasma exchange accompanied by a single administration of rituximab. The case of rejection was refractory to repeated steroid pulse treatment, intravenous immunoglobulin administration and intensifying immunosuppression.

Kaczorowski, DJ et al. (2013). Profound hyperacute cardiac allograft rejection rescue with biventricular mechanical circulatory support and plasmapheresis, intravenous immunoglobulin, and rituximab therapy. *Journal of Cardiothoracic Surgery*, 8:48. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23497431>

- This is a case report of hyperacute rejection managed with ventricular assist devices (VADs) for biventricular support during treatment with rituximab, intravenous immunoglobulin (IVIG), and plasmapheresis.

Chandola, R et al. (2012). Use of Impella 5L for Acute Allograft Rejection Postcardiac Transplant. *Thorac Cardiovasc Surg*, 60, 302–304. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22547305>

- This is a case report of rejection despite inotropes and immunosuppression managed with an Impella LP 5.0.

Velez-Martinez, M et al. (2011). Successful Use of the TandemHeart Percutaneous Ventricular Assist Device as a Bridge to Recovery for Acute Cellular Rejection in a Cardiac Transplant Patient. *Transplantation Proceedings*, 43, 3882–3884. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22172864>

- This is a case report of a TandemHeart Percutaneous Ventricular Assist Device being used to manage acute cellular rejection.

Thomas, HL et al. (2011). Incidence and outcome of Levitronix CentriMag support as rescue therapy for early cardiac allograft failure: a United Kingdom national study. *European Journal of Cardio-thoracic Surgery*, 40, 1348—1354. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/21493083>

- This is a retrospective study analyzing the effect of using Levitronix CentriMag mechanical circulatory support as therapy for rejection and its effect on survival and graft failure.

Jhang, J et al. (2007). Therapeutic Plasma Exchange Performed in Parallel with Extra Corporeal Membrane Oxygenation for Antibody Mediated Rejection after Heart Transplantation. *Journal of Clinical Apheresis*, 22, 333–338. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/18080271>

- This is a case report demonstrating the use of therapeutic plasmapheresis in parallel with extracorporeal membrane oxygenation to alleviate antibody mediated rejection.

Kaczmarek, I et al. (2007). Successful Management of Antibody-Mediated Cardiac Allograft Rejection With Combined Immunoabsorption and Anti-CD20 Monoclonal Antibody Treatment: Case Report and Literature Review. *J Heart Lung Transplant*, 26, 511–5. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17449422>

- This is a case report of a patient with antibody mediated rejection who was successfully treated with 3 cycles of immunoabsorption and a single-dose administration of rituximab.

Garrett Jr., EH et al. (2005). Treatment of Vascular Rejection With Rituximab in Cardiac Transplantation. *J Heart Lung Transplant*, 24, 1337–42. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16143254>

- This is a case report of 8 patients with antibody mediated rejection successfully treated with rituximab at a dose of 375 mg/m² per week for 4 weeks.

Baran, DA et al. (2004). Refractory Humoral Cardiac Allograft Rejection Successfully Treated With a Single Dose of Rituximab. *Transplantation Proceedings*, 36, 3164–3166. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15686719>

- This is a case report of refractory humoral cardiac rejection successfully treated with a single dose of rituximab 375 mg/m².

Ankersmit, HJ et al. (2003). Rapamycin as Rescue Therapy in a Patient Supported by Biventricular Assist Device to Heart Transplantation With Consecutive Ongoing Rejection. *American Journal of Transplantation*, 3, 231—234. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/12603219>

- This is a case report of cardiac allograft rejection despite treatment with antithymocyte globulin (ATG), FK506, a mycophenolate switch and courses of multiple apheresis that was successfully treated with Rapamycin.

Ahualli, L et al. (2002). Combined Dialytic Therapy in the Treatment of Vascular Rejection After Heart Transplantation. *Transplantation Proceedings*, 34, 157–160. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11959230>

- This is a case report of cardiac allograft rejection treated with plasmapheresis, thymoglobulin, corticosteroids, cyclosporine, and cyclophosphamide.

Aranda, JM et al. (2002). Anti-CD20 Monoclonal Antibody (Rituximab) Therapy for Acute Cardiac Humoral Rejection: A Case Report. *Transplantation*, 73:6, 907–910. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11923690>

- This is a case report of humoral rejection resistant to steroids, cyclophosphamide, and plasmapheresis successfully treated with rituximab.

Lehrer, MS et al. (2001). Successful Reversal of Severe Refractory Cardiac Allograft Rejection by Photopheresis. *J Heart Lung Transplant*, 20:1233–1236. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11704486>

- This is a case report of 4 patients with refractory International Society of Heart and Lung Transplantation Grades IIIA to IV cardiac allograft rejection treated successfully with extracorporeal photopheresis.

Grauhan, O et al. (2001). Plasmapheresis and Cyclophosphamide in the Treatment of Humoral Rejection After Heart Transplantation. *J Heart Lung Transplant*, 20:316–321. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11257558>

- This is a retrospective study evaluating the use of corticosteroids and cytolytic antibodies vs. corticosteroids, cytolytic antibodies, and plasmapheresis to treat humoral rejection post heart transplant.

Patel, JK et al. (2004). Immunosuppression, Diagnosis, and Treatment of Cardiac Allograft Rejection. *Semin Thorac Cardiovasc Surg*, 16:378-385. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15635544>

- This is a review article that addresses immunosuppression post-transplant as well as the diagnosis and treatment of cardiac allograft rejection.

Patel, JK et al. (2011). Cardiac allograft rejection. *The Surgeon*, 9, 160-167. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/21550522>

- This article is a review of the current status of the diagnosis of cardiac allograft rejection as determined by the traditional endomyocardial biopsy, the more recent advances in the non-invasive evaluation of rejection, detection of circulating antibodies and the treatment of rejection.

Chih, S et al. (2013). A Survey of Current Practice for Antibody Rejection in Heart Transplantation. *American Journal of Transplantation*, 13:1069–1074. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23414257>

- This article reviewed and analyzed online survey data from 184 ISHLT members from medium to large volume adult transplant centers in North America and Europe to determine their practices regarding criteria for initiating treatment for rejection and the treatment of antibody mediated rejection.

Stewart, S et al. (2005). Revision of the 1990 Working Formulation for the Standardization of Nomenclature in the Diagnosis of Heart Rejection. *J Heart Lung Transplant*, 24:1710–20. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16297770>

- This is the ISHLT guidelines for diagnosis of rejection in heart transplant patients.

5.5. Retransplant/graft failure

Johnson MR, Aaronson KD, Canter CE, et al. Heart retransplantation. *Am J Transplant*. 2007;7:2075-2081. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17640316>

- A review article in which a working group developed recommendations, based on available data and expert opinion, concerning heart retransplantation.
- Summarized all relevant trials of retransplantation in adults and pediatrics
- One-year, three-year and five-year unadjusted graft survival was lower in retransplants than in first transplants (82% vs. 86%, 70% vs. 80%, & 58% vs. 73%, $p < 0.0001$, respectively).

Tjang TS, Tenderich G, Hornik L, Korfer R. Cardiac retransplantation in adults: an evidence-based systemic review. *Thorac Cardiovasc Surg*. 2008; 56:323-327. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/18704853>

- A systemic review of available evidence regarding cardiac retransplantation in adults.
- Scrutinized 22 published studies

5.6. Cardiac diseases

5.6.1. Cardiomyopathy

Braun M, Edelmann F, Knapp M, Schön S, Schwencke C, Simonis G, Borst M, Weinbrenner C, Strasser RH. (2009). The calcium channel blocker felodipine attenuates the positive hemodynamic effects of the beta-blocker metoprolol in severe dilated cardiomyopathy--a prospective, randomized, double-blind and placebo-controlled study with invasive hemodynamic assessment. *International Journal of Cardiology*, 32, 248-256.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/18579230>

- Patients receiving metoprolol experienced significantly improved LVEF, LVEDD as well as decreased PAP and PCWP. When combined with felodipine these benefits were negated.

Ermakov S, Hoffmayer KS, Gerstenfeld EP, Scheinman MM. (2014). Combination drug therapy for patients with intractable ventricular tachycardia associated with right ventricular cardiomyopathy. *Pacing and Clinical Electrophysiology*, 37, 90-94.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/24102153>

- Review of four RV cardiomyopathy cases with RV-originating ventricular arrhythmia refractory to monotherapy and/or ablation. Combination therapy with sotalol, flecainide and mexiletine was used to control arrhythmia.

Kaya MG, Sarli B, Akpek M, Kaya EG, Yarlioglu M, Topsakal R, Lam YY. (2014). Evaluation of beta-blockers on left ventricular dyssynchrony and reverse remodeling in idiopathic dilated cardiomyopathy: A randomized trial of carvedilol and metoprolol. *Cardiology Journal*, e-pub. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/24142686>

- Carvedilol was associated with greater reduction in LVEDV, increase in LVEF and improvement in inter-ventricular dyssynchrony compared to metoprolol. Both medications improved intraventricular dyssynchrony, reverse remodeling and BNP levels.

Lund, L. H. et al (2011). Myocardial recovery in peri-partum cardiomyopathy after continuous flow left ventricular assist device. *Journal of Cardiothoracic Surgery*, 6: 150.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22082339>

- Case report of peri-partum cardiomyopathy requiring LVAD that recovered and remains stable in NYHA class I-II 18 months post-explantation.

Rasmusson, K. D. (2007). Long-term Outcomes of Cardiac Transplantation for Peri-partum Cardiomyopathy: A Multiinstitutional Analysis. *Journal of Heart and Lung Transplantation*, 26, 1097-1104. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/18022074>

- Sixty-nine women who received a heart transplant for peri-partum cardiomyopathy (PPCM) were compared to males as well as females with and without history of pregnancy. Risk of rejection was greater for the PPCM group compared to males and females without previous pregnancy. Long-term survival for PPCM recipients was comparable to males and improved compared to other females.

Westhoff-Bleck, M. et al (2013). Cardiovascular Disorders in Pregnancy: Diagnosis and Management. *Best Practice & Research Clinical Obstetrics and Gynaecology*, 27, 821-834.

Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23932772>

- Summary of pathophysiology, diagnosis and treatment of cardiovascular disorders during pregnancy, including peri-partum cardiomyopathy.

5.6.2. Congenital heart disease

VanderPluym, C et al. (2013). Advanced Therapies for Congenital Heart Disease: Ventricular Assist Devices and Heart Transplantation. *Canadian Journal of Cardiology*, 29, 796-802. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23683470>

- This article reviews reasons for VAD implantation in congenital heart disease (CHD), VAD support in Fontan circulation, challenges with human leukocyte antigen sensitization in heart transplantation (HT), and the effect of VAD support on HT in CHD.

Kaufman, BD et al. (2011). Immunologic Considerations in Heart Transplantation for Congenital Heart Disease. *Current Cardiology Reviews*, 7, 67-71. Retrieved from

<http://www.ncbi.nlm.nih.gov/pubmed/22548029>

- This article reviews the causes of anti-HLA antibody production (allosensitization), preventive strategies for allosensitization before transplantation, treatment strategies for allosensitization before transplantation, consequences of HLA allosensitization after transplantation and treatment of HLA allosensitization and antibody-mediated rejection after transplantation.

Pincott, SE et al. (2011). Indications for Heart Transplantation in Congenital Heart Disease. *Current Cardiology Reviews*, 7, 51-58. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22548027>

- This article reviews the indications for transplantation in congenital heart disease, the timing of transplantation, as well as potential complications of transplantation in congenital heart disease.

McGlothlin, D et al. (2011). Transplantation in Adults With Congenital Heart Disease. *Progress in Cardiovascular Diseases*, 53, 312–323. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/21295673>

- This article addresses some of the unique challenges to transplantation and post-transplant management in congenital heart disease.

Hosseinpour, A et al. (2006). Transplantation for adults with congenital heart disease. *European Journal of Cardio-thoracic Surgery*, 30, 508—514. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16857376>

- This article reviews indications for transplantation in congenital heart disease and addresses unique considerations and complications to transplant.

5.6.3. Coronary artery disease

Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patient with stable ischemic heart disease. *J Am Coll Cardiol*; 60(24):1-121. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/23182125>

- Guidelines published by ACCF/AHA/American College of Physicians (ACP)/American Association for Thoracic Surgery (AATS)/Preventive Cardiovascular Nurses Association (PCNA)/Society of Cardiovascular Angiography and Interventions (SCAI)/and Society of Thoracic Surgeons (STS) on the diagnosis and management of patients with stable ischemic heart disease.

Kato T, Chan MCY, Gao S-Z, et al. Glucose intolerance, as reflected by hemoglobin A1c level, is associated with the incidence and severity of transplant coronary artery disease. *J Am Coll Cardiol*. 2004; 43:1034-41. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/15028363>

- Examined the association between transplant CAD and established risk factors.

- Results: Chronic mild elevations of plasma glucose in heart transplant patients may contribute to the development of transplant CAD.

Smith SC, Benjamin EJ, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the AHA and ACCF. *Circulation*. 2011; 124:2458-2473. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22052934>

- Guidelines published by the American Heart Association (AHA)/American College of Cardiology Foundation (ACCF) on secondary prevention and risk reduction in patients with established coronary and atherosclerotic vascular disease, including peripheral artery disease, atherosclerotic aortic disease, and carotid artery disease.

5.6.4. Valvular heart disease

Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 Guidelines for the management of patients with valvular heart disease. *Circulation*. 2006; 114:e84-e231. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16880336>

- Guidelines published by American College of Cardiology (ACC) and AHA on general issues of treatment of patients with heart valve disorders, such as evaluation of patients with heart murmurs, prevention and treatment of endocarditis, management of valve disease in pregnancy, and treatment of patients with concomitant coronary artery disease (CAD), as well as more specialized issues that pertain to specific valve lesions.

Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012). *European Heart Journal*. 2012; 33:2451-2496. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/22922415>

- Guidelines published by the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) on management of acquired valvular heart disease.
- These were the most recent guidelines available for valvular heart disease.

Reference Review – Heart Transplant (1/1/15 – 3/31/17)

Grimm JC, Magruder JT, Crawford TC, et al. Duration of Left Ventricular Assist Device Support Does Not Impact Survival After US Heart Transplantation. *Ann Thorac Surg*. 2016; 102(4):1206-12. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27319984>

- In the largest, non-industry sponsored study of a modern bridge to transplant cohort, this study demonstrated that duration of LVAD support before orthotopic heart transplantation does not influence posttransplant morbidity or mortality. In subanalysis, support for 90 days or more is associated with improvements in pretransplant functional performance.

Vallakati A, Reddy S, Dunlap ME, Taylor DO. Impact of Statin Use After Heart Transplantation: A Meta-Analysis. *Circ Heart Fail*. 2016 Oct;9(10). Retrieved from:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Impact+of+Statin+Use+After+Heart+Transplantation%3A+A+Meta-Analysis>.

- The evidence from a pooled analysis suggests that statins improve survival in heart transplant recipients. Statins may prevent fatal rejection episodes, decrease terminal cancer risk, and reduce the incidence of coronary vasculopathy. Additional prospective studies are needed to further investigate and explain this association.

Sierra CM(1), Tan R(2), Eguchi J(3), Bailey L(4), Chinnock RE(3). Calcineurin inhibitor- and corticosteroid-free immunosuppression in pediatric heart transplant patients. *Pediatr Transplant*. 2016 Sep 23. doi: 10.1111/ptr.12808. [Epub ahead of print]. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27658616>

- Immunosuppression free of CNIs and corticosteroids appears to be a safe alternative in pediatric heart transplant patients with significant renal insufficiency. Furthermore, this strategy can significantly reverse renal insufficiency, even late after transplantation.

Sarmiento E, Diez P, Arraya M, et al. Early intravenous immunoglobulin replacement in hypogammaglobulinemic heart transplant recipients: results of a clinical trial. *Transpl Infect Dis*. 2016 Sep 17. doi: 10.1111/tid.12610. [Epub ahead of print]. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Early+intravenous+immunoglobulin+replacement+in+hypogammaglobulinemic+heart+transplant+recipients%3A+results+of+a+clinical+trial>.

- Data from this study demonstrate that prophylactic IVIG replacement therapy safely modulates HGG and specific antimicrobial antibodies. This data also preliminarily suggest that IVIG replacement therapy might decrease the incidence of severe infection in heart recipients with HGG.

Ciarka A, Lund LH, Van Cleemput J, Voros G, Droogne W, Vanhaecke J. Effect of Heart Rate and Use of Beta Blockers on Mortality After Heart Transplantation. *Am J Cardiol*. 2016 Sep 15. pii: S0002-9149(16)31500-4. doi: 10.1016/j.amjcard.2016.08.084. [Epub ahead of print]. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Effect+of+Heart+Rate+and+Use+of+Beta+Blockers+on+Mortality+After+Heart+Transplantation>.

- In a large single-center cohort of HT recipients, higher heart rate and nonuse of β blockers were independently associated with higher mortality.

Mirza K(1), Gustafsson F(2), Gullestad L(3), Arora S(3), Andersen C(4). Effect of everolimus initiation and early calcineurin inhibitor withdrawal on myocardial FOXP3+ regulatory T cells in heart transplantation. *Transpl Immunol*. 2016 Sep;38:75-7. doi: 10.1016/j.trim.2016.05.004. Epub 2016 May 31. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Effect+of+everolimus+initiation+and+earl>

[y+calcineurin+inhibitor+withdrawal+on+myocardial+FOXP3%2B+regulatory+T+cells+in+heart+transplantation.](#)

- Everolimus treatment combined with early CNI elimination is associated with increased densities of Tregs 12-months post-HTx compared to patients receiving CNI based regimen. Furthermore, the density of myocardial FoxP3+ cells early after transplantation appears to predict at least one measure of CAV burden after one year.

Chih S, Patel J. Desensitization strategies in adult heart transplantation-Will persistence pay off? J Heart Lung Transplant. 2016 Aug;35(8):962-72. doi:10.1016/j.healun.2016.03.021.

Epub 2016 Mar 31. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Desensitization+strategies+in+adult+heart+transplantation-Will+persistence+pay+off%3F>

- Review article of desensitization strategies in adult heart transplantation. No approach has demonstrated significant and sustainable reductions in HLA antibody pre-transplant, and the ideal desensitization strategy remains elusive. In addition, clinical tools to evaluate the humoral response and efficacy of therapy are limited, focusing almost exclusively on HLA antibody detection. Importantly, desensitization is associated with significant costs and potential risks, and overall long-term outcomes and cost-effectiveness have not been sufficiently evaluated.

Quintana-Quezada RA, Rajapreyar I, Postalian-Yrausquin A, et al. Clinical Factors Implicated in Primary Graft Dysfunction After Heart Transplantation: A Single-center Experience. Transplant Proc. 2016 Jul-Aug;48(6):2168-71. doi:

10.1016/j.transproceed.2016.02.073. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Clinical+Factors+Implicated+in+Primary+Graft+Dysfunction+After+Heart+Transplantation%3A+A+Single-center+Experience.>

- This study showed that a longer time from brain death to aortic cross clamp was associated with lower odds of developing PGD. Therefore, postponing heart procurement for a few days after brain death seems to be beneficial in preventing PGD.

Andreassen AK, Andersson B, Gustafsson F, et al. Everolimus Initiation With Early Calcineurin Inhibitor Withdrawal in De Novo Heart Transplant Recipients: Three-Year Results From the Randomized SCHEDULE Study. Am J Transplant. 2016 Apr;16(4):1238-47. doi: 10.1111/ajt.13588. Epub 2016 Jan 28. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Everolimus+Initiation+With+Early+Calcineurin+Inhibitor+Withdrawal+in+De+Novo+Heart+Transplant+Recipients%3A+Three-Year+Results+From+the+Randomized+SCHEDULE+Study.>

- In a randomized, open-label trial, de novo heart transplant recipients were randomized to everolimus with reduced-exposure calcineurin inhibitor to weeks 7-11 after transplant, followed by increased everolimus exposure with cyclosporine withdrawal or standard-exposure cyclosporine. Early CNi withdrawal after heart transplantation supported by everolimus, mycophenolic acid and steroids with lymphocyte-depleting induction was shown to be safe at intermediate follow-up. This regimen, used selectively, may offer adequate immunosuppressive potency with a sustained renal advantage, however, at the risk of increased biopsy proven acute rejection.

Wang YJ, Chi NH, Chou NK, et al. Malignancy After Heart Transplantation Under Everolimus Versus Mycophenolate Mofetil Immunosuppression. *Transplant Proc.* 2016 Apr;48(3):969-73. doi: 10.1016/j.transproceed.2015.12.071. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Malignancy+After+Heart+Transplantation+Under+Everolimus+Versus+Mycophenolate+Mofetil+Immunosuppression>.

- EVR treatment after heart transplant is associated with a lower risk of malignancy than is MMF treatment. The 2-year survival rate after malignancy was similar between EVR and MMF groups.

Kfoury AG, Miller DV, Snow GL, et al. Mixed cellular and antibody-mediated rejection in heart transplantation: In-depth pathologic and clinical observations. *J Heart Lung Transplant.* 2016 Mar;35(3):335-41. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Mixed+cellular+and+antibody-mediated+rejection+in+heart+transplantation%3A+In-depth+pathologic+and+clinical+observations>.

- Mixed rejection is not common, usually occurs early after transplant, and is associated with worse outcomes. Mixed rejection reflects a complex interplay between cellular and humoral processes, which varies with rejection severity.

Aliabadi AZ(1), Grömmer M, Dunkler D, et al. Impact of Rabbit Antithymocyte Globulin Dose on Long-term Outcomes in Heart Transplant Patients. *Transplantation.* 2016 Mar;100(3):685-93. doi: 10.1097/TP.0000000000000950. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Impact+of+Rabbit+Antithymocyte+Globulin+Dose+on+Long-term+Outcomes+in+Heart+Transplant+Patients>.

- This retrospective data suggest that a cumulative rATG dose of 4.5 to 7.5 mg/kg may offer a better risk-benefit ratio than lower or higher doses, with acceptable rates of infection and posttransplant malignancy. Prospective trials are needed.

Watanabe T, Seguchi O, Nishimura K, et al. Suppressive effects of conversion from mycophenolate mofetil to everolimus for the development of cardiac allograft vasculopathy in maintenance of heart transplant recipients. *Int J Cardiol.* 2016 Jan 15;203:307-14. doi: 10.1016/j.ijcard.2015.10.082. Epub 2015 Oct 23. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Suppressive+effects+of+conversion+from+mycophenolate+mofetil+to+everolimus+for+the+development+of+cardiac+allograft+vasculopathy+in+maintenance+of+heart+transplant+recipients>.

- Conversion to EVL from MMF in maintenance periods after HTx may decrease the rate of CAV progression based on IVUS indices.

Agüero F, Castel MA, Cocchi S, et al. An Update on Heart Transplantation in Human Immunodeficiency Virus-Infected Patients. *Am J Transplant.* 2016 Jan;16(1):21-8. doi: 10.1111/ajt.13496. Epub 2015 Nov 2. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=An+Update+on+Heart+Transplantation+in+Human+Immunodeficiency+Virus-Infected+Patients>.

- This review article analyzes epidemiological data on ESHF in HIV-infected patients from all published experience on HT in HIV-infected patients since the beginning of the epidemic. The practical management of these patients is discussed, with emphasis on the challenging issues that must be addressed in the pretransplant (including HIV criteria) and posttransplant periods.

Azarbal B, Cheng R, Vanichsarn C, et al. Induction Therapy With Antithymocyte Globulin in Patients Undergoing Cardiac Transplantation Is Associated With Decreased Coronary Plaque Progression as Assessed by Intravascular Ultrasound. *Circ Heart Fail.* 2016 Jan;9(1):e002252. doi: 10.1161/CIRCHEARTFAILURE.115.002252. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Induction+Therapy+With+Antithymocyte+Globulin+in+Patients+Undergoing+Cardiac+Transplantation+Is+Associated+With+Decreased+Coronary+Plaque+Progression+as+Assessed+by+Intravascular+Ultrasound>.

- Induction therapy with ATG is associated with reduced first-year coronary plaque progression as assessed by IVUS, despite an increased prevalence of sensitized patients with a trend toward more rejection.

Mehra MR, Canter CE, Hannan MM, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update. *J Heart Lung Transplant.* 2016 Jan;35(1):1-23. doi: 10.1016/j.healun.2015.10.023. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=The+2016+International+Society+for+Heart+Lung+Transplantation+listing+criteria+for+heart+transplantation%3A+A+10-year+update>

- Review of the ISHLT listing criteria for heart transplantation

Tran A, Fixler D, Huang R, Meza T, Lacelle C, Das BB. Donor-specific HLA alloantibodies: Impact on cardiac allograft vasculopathy, rejection, and survival after pediatric heart transplantation. *J Heart Lung Transplant*. 2016 Jan;35(1):87-91. doi: 10.1016/j.healun.2015.08.008. Epub 2015 Sep 3. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Donor-specific+HLA+alloantibodies%3A+Impact+on+cardiac+allograft+vasculopathy%2C+rejection%2C+and+survival+after+pediatric+heart+transplantation>

- Of the 105 patients, 45 (43%) developed de novo DSA. DSA-positive patients had significantly higher rates of coronary artery vasculopathy (CAV) compared with DSA-negative patients (36% vs 13%). The 5-year graft survival rate was 72.4% for DSA-negative patients and 21% for DSA-positive patients (< 0.001). De novo DSA has a strong negative impact on CAV, rejection, and graft survival in pediatric recipients of heart transplants.

Healy AH, Stehlik J, Edwards LB, McKellar SH, Drakos SG, Selzman CH. Predictors of 30-day post-transplant mortality in patients bridged to transplantation with continuous-flow left ventricular assist devices--An analysis of the International Society for Heart and Lung Transplantation Transplant Registry. *J Heart Lung Transplant*. 2016 Jan;35(1):34-9. doi: 10.1016/j.healun.2015.07.007. Epub 2015 Jul 29. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Predictors+of+30-day+post-transplant+mortality+in+patients+bridged+to+transplantation+with+continuous-flow+left+ventricular+assist+devices--an+analysis+of+the+International+Society+for+Heart+and+Lung+Transplantation+Transplant+Registry>

- In patients supported with continuous flow LVADs, risk factors for early mortality can be identified before transplant, including ventilator support, female recipient/male donor, increasing recipient age, and body mass index. Despite the inherent complexities of a reoperative surgery, patients bridged to transplant with CF LVADs have excellent peri-operative survival.

Ansari D, Höglund P, Andersson B, Nilsson J. Comparison of Basiliximab and Anti-Thymocyte Globulin as Induction Therapy in Pediatric Heart Transplantation: A Survival Analysis. *J Am Heart Assoc*. 2015 Dec 31;5(1). pii: e002790. doi: 10.1161/JAHA.115.002790. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Comparison+of+Basiliximab+and+Anti-Thymocyte+Globulin+as+Induction+Therapy+in+Pediatric+Heart+Transplantation%3A+A+Survival+Analysis>

- In pediatric heart transplant patients, use of basiliximab for induction therapy was associated with an increased risk of mortality, when compared with those receiving anti-thymocyte globulin.

Foster BJ, Dahhou M, Zhang X, et al. High Risk of Graft Failure in Emerging Adult Heart Transplant Recipients. *Am J Transplant*. 2015 Dec;15(12):3185-93. doi: 10.1111/ajt.13386. Epub 2015 Jul 16. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/26189336>.

- Crude age-specific graft failure rates were highest in 21-24 year olds (4.2 per 100 person-years). Compared to individuals with the same time since transplant, 21-24 year olds had significantly higher failure rates than all other age periods except 17-20 years (HR 0.92 [95%CI 0.77, 1.09]) and 25-29 years (0.86 [0.73, 1.03]). Among young first heart transplant recipients, graft failure risks are highest in the period from 17 to 29 years of age.

Lesche D, Sigurdardottir V, Setoud R, et al. Influence of CYP3A5 genetic variation on everolimus maintenance dosing after cardiac transplantation. *Clin Transplant*. 2015 Dec;29(12):1213-20. doi: 10.1111/ctr.12653. Epub 2015 Nov 23. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Influence+of+CYP3A5+genetic+variation+on+everolimus+maintenance+dosing+after+cardiac+transplantation>.

- Everolimus pharmacokinetics in HTx recipients is highly variable. This preliminary data on patients on a CNI-free therapy regimen suggest that CYP3A5 genetic variation may contribute to this variability.

Godown J(1), Slaughter JC(2), Fossey SC(3), McKane M(1), Dodd DA(1). Risk factors for the development of donor-specific antibodies after pediatric heart transplantation. *Pediatr Transplant*. 2015 Dec;19(8):906-10. doi: 10.1111/petr.12606. Epub 2015 Sep 28. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/26412798>

- De novo DSA were detected in 40 (33%) of 121 HTx recipients. Characteristics associated with de novo DSA included older age, African American race, prior operations, prior ECMO, PRA > 10%, longer bypass time, mechanical support at transplant, and donor death from GSW. In a multivariable model, mechanical support (HR 3.23, 95% CI [1.02, 8.87]), African American race (HR 3.36, 95% CI [1.68, 7.32]), and donor death from GSW (HR 4.76, 95% CI [1.62, 14.01]) were significantly associated with DSA. Multiple factors appear to play a role in the development of DSA, knowledge of which may guide the frequency of post-transplant monitoring. DSA develop more frequently in those with prior sensitizing events, suggesting the possibility that these exposures predispose the immune system to respond to donor antigens, even in the presence of a negative cross-match.

Qiu Y, Wang X, Fan J, Rao Z, Lu Y, Lin T. Conversion From Calcineurin Inhibitors to Mammalian Target-of-Rapamycin Inhibitors in Heart Transplant Recipients: A Meta-Analysis of Randomized Controlled Trials. *Transplant Proc*. 2015 Dec;47(10):2952-6. doi: 10.1016/j.transproceed.2015.09.059. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Conversion+From+Calcineurin+Inhibitors>

[+to+Mammalian+Target-of-Rapamycin+Inhibitors+in+Heart+Transplant+Recipients%3A+A+Meta-Analysis+of+Randomized+Controlled+Trials.](#)

- Conversion from CNI to mTORi therapy may improve the renal function in HTRs, but the patients may suffer from a high incidence of mTORi-associated adverse events. Therefore, conversion to mTORi must be carefully assessed for the benefits and risks.

Jansen MA, Otten HG, de Weger RA, Huibers MM. Immunological and Fibrotic Mechanisms in Cardiac Allograft Vasculopathy. *Transplantation*. 2015 Dec;99(12):2467-75. doi: 10.1097/TP.0000000000000848. Retrieved from:

<https://www.ncbi.nlm.nih.gov/pubmed/26285017>

- A review of the data on the immunological and fibrotic processes that are involved in the development of CAV are summarized. Areas where a lack of knowledge exists and possible additional research can be completed are pinpointed. During the pathogenesis of CAV, cells from the innate and the adaptive immune system cooperate to reject the foreign heart. This inflammatory response results in dysfunction of the endothelium and migration and proliferation of smooth muscle cells (SMCs). Apoptosis and factors secreted by both the endothelium as well as the SMCs lead to fibrosis. The migration of SMCs together with fibrosis provoke concentric intimal thickening of the coronary arteries, which is the main characteristic of CAV.

Grimm JC, Kilic A, Shah AS, et al. The influence of institutional volume on the incidence of complications and their effect on mortality after heart transplantation. *J Heart Lung Transplant*. 2015 Nov;34(11):1390-7. doi: 10.1016/j.healun.2015.05.014. Epub 2015 Jun 10. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=The+influence+of+institutional+volume+on+the+incidence+of+complications+and+their+effect+on+mortality+after+heart+transplantation.>

- Postoperative complications after OHT have a greater incidence and effect on short-term and long-term survival at low-volume institutions. Accordingly, best practice guidelines established at high-volume institutions could better equip lower-volume hospitals to manage these events in hopes of optimizing transplant outcomes.

Kumarasinghe G, Lavee O, Parker A, et al. Post-transplant lymphoproliferative disease in heart and lung transplantation: Defining risk and prognostic factors. *J Heart Lung Transplant*. 2015 Nov;34(11):1406-14. doi: 10.1016/j.healun.2015.05.021. Epub 2015 Jun 11. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/26279197>

- This analysis is the largest to date on PTLN in heart and lung transplant recipients. It provides a detailed analysis of the disease in this group of patients and identifies unique prognostic features to aid risk stratification and guide treatment allocation.

Mateo R, Gupta S, Wallia A, et al. Relationship Between Hyperglycemia and Heart Transplant Rejection. *Transplant Proc.* 2015 Nov;47(9):2727-31. doi:

10.1016/j.transproceed.2015.09.063. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/26680082>

- Grade $\leq 1R$ rejection on biopsy was observed in 116 patients and grade $\geq 2R$ rejection (grade requiring increased anti-rejection treatment) in 41 patients. Although no significant differences in the preoperative fasting or inpatient mean glucose levels were found, the mean glucose levels from discharge to 1 year trended higher in those with grade $\geq 2R$ compared to grade $\leq 1R$ (128.8 ± 40.9 versus 142.2 ± 46.6 mg/dL, $P = .084$).

Ansari D, Bućin D, Höglund P, Ohlsson M, Andersson B, Nilsson J. Analysis of the Influence of HLA-A Matching Relative to HLA-B and -DR Matching on Heart Transplant Outcomes. *Transplant Direct.* 2015 Oct 19;1(9):e38. doi:

10.1097/TXD.0000000000000545.eCollection 2015. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Analysis+of+the+Influence+of+HLA-A+Matching+Relative+to+HLA-B+and+-DR+Matching+on+Heart+Transplant+Outcomes>.

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Analysis+of+the+Influence+of+HLA-A+Matching+Relative+to+HLA-B+and+-DR+Matching+on+Heart+Transplant+Outcomes>.

- Decreased long-term survival in heart transplantation was associated with HLA-A compatibility in HLA-B,DR-incompatible grafts.

Andrew J, Macdonald P. Latest developments in heart transplantation: a review. *Clin Ther.* 2015 Oct 1;37(10):2234-41. doi: 10.1016/j.clinthera.2015.08.019. Retrieved at:

10.1016/j.clinthera.2015.08.019. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/26497799>

- A review of recently published literature in heart transplant.

Rosenbaum AN, Edwards BS. Current indications, strategies, and outcomes with cardiac transplantation for cardiac amyloidosis and sarcoidosis. *Curr Opin Organ Transplant.* 2015 Oct;20(5):584-92. doi:10.1097/MOT.0000000000000229. Retrieved at:

10.1097/MOT.0000000000000229. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Current+indications%2C+strategies%2C+and+outcomes+with+cardiac+transplantation+for+cardiac+amyloidosis+and+sarcoidosis>.

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Current+indications%2C+strategies%2C+and+outcomes+with+cardiac+transplantation+for+cardiac+amyloidosis+and+sarcoidosis>.

- Outcomes after heart transplantation are typically worse than in patients undergoing heart transplantation for nonamyloid disease. This review analyzes the indications, strategies and outcomes in patients with amyloidosis and sarcoidosis.

Chang DH, Kobashigawa JA. Current diagnostic and treatment strategies for cardiac allograft vasculopathy. *Expert Rev Cardiovasc Ther.* 2015 Oct;13(10):1147-54.

doi:10.1586/14779072.2015.1087312. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/26401922>

- Review of current strategies in diagnosing and treating cardiac allograft vasculopathy

Irving CA, Carter V, Gennery AR, et al. Effect of persistent versus transient donor-specific HLA antibodies on graft outcomes in pediatric cardiac transplantation. *J Heart Lung Transplant*. 2015 Oct;34(10):1310-7. doi: 10.1016/j.healun.2015.05.001. Epub 2015 May 8. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Effect+of+persistent+versus+transient+donor-specific+HLA+antibodies+on+graft+outcomes+in+pediatric+cardiac+transplantation>.

- De novo HLA antibodies are detectable post-transplant in the majority of patients, but non-DSA and transient DSA do not appear to be associated with poor outcomes. Patients with persistent DSA, especially those with Class II DQ antibodies, have worse survival.

Ansari D, Lund LH, Stehlik J, et al. Induction with anti-thymocyte globulin in heart transplantation is associated with better long-term survival compared with basiliximab. *J Heart Lung Transplant*. 2015 Oct;34(10):1283-91. doi:10.1016/j.healun.2015.04.001. Epub 2015 May 2. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Induction+with+anti-thymocyte+globulin+in+heart+transplantation+is+associated+with+better+long-term+survival+compared+with+basiliximab>

- A total of 9,324 transplantations performed between 2000 and 2011 whose recipients received ATG (n = 6,144) or BAS (n = 3,180). One-year survival was similar for both groups, 90% vs 91% (p = 0.858). However, use of BAS was associated with poorer long-term survival compared with ATG at 5 years (77% vs 82%, p = 0.005) and at 10 years (64% vs 67%, p = 0.007). In multivariable Cox model, use of BAS remained associated with increased mortality over a median follow-up of 3.0 years (range, 0-12 years), with a hazard ratio of 1.22 (95% confidence interval, 1.09-1.37; p < 0.001). The use of ATG rather than BAS as induction therapy appears to be associated with better long-term survival. A prospective study is necessary to confirm these findings.

Marcelino CA(1), Díaz LJ, da Cruz DM. The effectiveness of interventions in managing treatment adherence in adult heart transplant patients: a systematic review. *JBIS Database System Rev Implement Rep*. 2015 Sep;13(9):279-308. doi:10.11124/jbisrir-2015-2288. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=The+effectiveness+of+interventions+in+managing+treatment+adherence+in+adult+heart+transplant+patients%3A+a+systematic+review>.

- Three quasi-experimental studies were included in this review. One study found that a dose reduction of immunosuppressive medications from a twice-daily to a once-daily regimen had a positive impact on treatment adherence; one found no significant difference in treatment adherence between patients who received educational intervention conducted in a teaching laboratory and those who received standard care; the third one also reported no significant difference in outcomes between a multifaceted intervention consisting of internet-based interactive workshops and standard care. There is weak evidence that psycho-educational interventions (other than the standard care) has a positive impact on adherence and that decreasing the complexity of the treatment regimen by reducing the daily dose of the immunosuppressant drug improves adherence in heart transplant patients.

Woillard JB, Saint-Marcoux F, Monchaud C, Youdarène R, Pouche L, Marquet P. Mycophenolic mofetil optimized pharmacokinetic modelling, and exposure-effect associations in adult heart transplant recipients. *Pharmacol Res.* 2015 Sep;99:308-15. doi: 10.1016/j.phrs.2015.07.012. Epub 2015 Jul 17. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Mycophenolic+mofetil+optimized+pharmacokinetic+modelling%2C+and+exposure-effect+associations+in+adult+heart+transplant+recipients>.

- MPA measured AUC adjusted on CNI exposure was significantly associated with rejection (per unit increase: HR [95% CI]=0.97 [0.95-0.99], p=0.0122), while no effect was shown for adverse events attributable to MMF. An AUC threshold of 50 mg×h/L was proposed (sensitivity=77%, specificity=25%) beyond which the risk of rejection was significantly increased (low vs. high: HR=3.48 [1.21-10.0], p=0.0204).

Chen CK, Manlhiot C, Conway J, et al. Development and Impact of De Novo Anti-HLA Antibodies in Pediatric Heart Transplant Recipients. *Am J Transplant.* 2015 Aug;15(8):2215-22. doi: 10.1111/ajt.13259. Epub 2015 Mar 17. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/25784138>

- Acute cellular rejection, though frequent, was not different in patients with antibody development regardless of class or specificity, and there was no antibody-mediated rejection, graft loss or early cardiac allograft vasculopathy.

Auerbach SR, Kukreja M, Gilbert D, et al. Maintenance steroid use at 30 days post-transplant and outcomes of pediatric heart transplantation: A propensity matched analysis of the Pediatric Heart Transplant Study database. *J Heart Lung Transplant.* 2015 Aug;34(8):1066-72. doi: 10.1016/j.healun.2015.03.003. Epub 2015 Mar 20. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Maintenance+steroid+use+at+30+days+post->

[transplant+and+outcomes+of+pediatric+heart+transplantation%3A+A+propensity+matched+analysis+of+the+Pediatric+Heart+Transplant+Study+database.](#)

- Maintenance steroid use at 30 days post-transplant was not associated with enhanced graft survival after pediatric heart transplant. Maintenance steroid patients had a higher incidence of rejection with severe hemodynamic compromise and infection. These risks should be taken into consideration when determining maintenance steroid use for pediatric recipients of heart transplants.

Coutance G, Ouldamar S, Rouvier P, et al. Late antibody-mediated rejection after heart transplantation: Mortality, graft function, and fulminant cardiac allograft vasculopathy. *J Heart Lung Transplant*. 2015 Aug;34(8):1050-7. doi:10.1016/j.healun.2015.03.002. Epub 2015 Mar 20. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Late+antibody-mediated+rejection+after+heart+transplantation%3A+Mortality%2C+graft+function%2C+and+fulminant+cardiac+allograft+vasculopathy>.

- Prognosis after late AMR is poor despite aggressive immunosuppressive therapies. Fulminant CAV is a common condition in these patients. Microvascular inflammation is frequent in endomyocardial biopsy specimens before manifestation of symptomatic AMR.

Delgado JF, Reyne AG, de Dios S, et al. Influence of cytomegalovirus infection in the development of cardiac allograft vasculopathy after heart transplantation. *J Heart Lung Transplant*. 2015 Aug;34(8):1112-9. doi: 10.1016/j.healun.2015.03.015. Epub 2015 Mar 26. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/25940077>.

- Standardized angiographic criteria show CMV infection is associated with the development of CAV

Durante-Mangoni E, Andini R, Pinto D, et al. Effect of the immunosuppressive regimen on the incidence of cytomegalovirus infection in 378 heart transplant recipients: A single centre, prospective cohort study. *J Clin Virol*. 2015 Jul;68:37-42. doi: 10.1016/j.jcv.2015.04.017. Epub 2015 Apr 22. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Effect+of+the+immunosuppressive+regimen+on+the+incidence+of+cytomegalovirus+infection+in+378+heart+transplant+recipients%3A+A+single+centre%2C+prospective+cohort+study>.

- Use of everolimus was associated with a significantly lower rate of CMV infection compared to azathioprine or mycophenolate (OR 0.19, 95% C.I. 0.09-0.39; p<0.0001)

Kidambi S, Mohamedali B, Bhat G. Clinical outcomes in sensitized heart transplant patients bridged with ventricular assist devices. *Clin Transplant*. 2015 Jun;29(6):499-505. doi: 10.1111/ctr.12540. Epub 2015 Apr 30. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Clinical+outcomes+in+sensitized+heart+transplant+patients+bridged+with+ventricular+assist+devices>.

- Sensitization appears to have a negative effect on mortality. This mortality appears to be concentrated in patients with AMR, and the authors postulate that the development of AMR in a sensitized patient may be a predictor of mortality.

Morris AA, Kalogeropoulos AP, Zhao L, et al. Race and ethnic differences in the epidemiology and risk factors for graft failure after heart transplantation. *J Heart Lung Transplant*. 2015 Jun;34(6):825-31. doi: 10.1016/j.healun.2014.12.012. Epub 2014 Dec 24. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/25682551>

- Black HT recipients have the highest risk of GF, with immunologic factors conferring the greatest proportion of that risk. Racial differences in risk factors for GF after HT require further study.

Gazdic T, Svobodova E, Kubanek M, et al. Bortezomib-containing regimen for primary treatment of early antibody-mediated cardiac allograft rejection: a case report. *Prog Transplant*. 2015 Jun;25(2):147-52. doi: 10.7182/pit2015934. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Bortezomib-containing+regimen+for+primary+treatment+of+early+antibody-mediated+cardiac+allograft+rejection%3A+a+case+report>.

- Primary treatment with a bortezomib-containing regimen appears to be a new therapeutic option for severe antibody-mediated rejection in heart transplant recipients.

Patel J, Klapper E, Shafi H, Kobashigawa JA. Extracorporeal photopheresis in heart transplant rejection. *Transfus Apher Sci*. 2015 Apr;52(2):167-70. doi: 10.1016/j.transci.2015.02.004. Epub 2015 Feb 11. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/25748232>.

- Extracorporeal photopheresis (ECP) appears particularly useful in the management of select heart transplant recipients at risk of rejection, with recurrent rejection, or rejection associated with hemodynamic compromise. This summarizes the current clinical experience of ECP in heart transplantation.

Zuckermann A, Schulz U, Deuse T, et al. Thymoglobulin induction in heart transplantation: patient selection and implications for maintenance immunosuppression. *Transpl Int*. 2015 Mar;28(3):259-69. doi: 10.1111/tri.12480. Epub 2014 Nov 11. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Thymoglobulin+induction+in+heart+transplantation%3A+patient+selection+and+implications+for+maintenance+immunosuppression>.

- Experts from Germany, Austria, and Switzerland convened to identify indications for rATG induction in heart transplantation and to develop an algorithm for its use based on patient characteristics.

Feingold B, Webber SA, Bryce CL, et al. Comparison of listing strategies for allosensitized heart transplant candidates requiring transplant at high urgency: a decision model analysis. *Am J Transplant*. 2015 Feb;15(2):427-35. doi: 10.1111/ajt.13071. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Comparison+of+listing+strategies+for+allosensitized+heart+transplant+candidates+requiring+transplant+at+high+urgency%3A+a+d+ecision+model+analysis>.

- A Markov decision model was created to compare survival after listing with a requirement for a negative prospective donor cell crossmatch (WAIT) versus acceptance of the first suitable offer (TAKE). Model parameters were derived from registry data on status 1A (highest urgency) pediatric heart transplant listings. Under base-case assumptions, TAKE showed an incremental survival benefit of 1.4 years over WAIT. In multiple sensitivity analyses, including variation of the probability of a positive crossmatch from 10% to 100%, TAKE was consistently favored. While model input data were less well suited to comparing survival when awaiting transplantation across a negative virtual crossmatch, this analysis suggests that taking the first suitable organ offer under these circumstances is also favored.

Rabin AS, Givertz MM, Couper GS, et al. Risk factors for invasive fungal disease in heart transplant recipients. *J Heart Lung Transplant*. 2015 Feb;34(2):227-32. doi: 10.1016/j.healun.2014.09.036. Epub 2014 Oct 2. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/25455750>

- Invasive fungal disease incidence was greatest within the first 3 months post-HT, largely reflecting early surgical-site and nosocomial *Candida* and *Aspergillus* infections. Patients receiving additional induction immunosuppression or delayed chest closure were at increased risk for IFD. Peri-transplant anti-fungal prophylaxis should be considered in this subset of HT recipients.

Alvarez-Alvarez RJ, Barge-Caballero E, Chavez-Leal SA, et al. Venous thromboembolism in heart transplant recipients: incidence, recurrence and predisposing factors. *J Heart Lung Transplant*. 2015 Feb;34(2):167-74. doi:10.1016/j.healun.2014.09.039. Epub 2014 Oct 2. Retrieved at: <https://www.ncbi.nlm.nih.gov/pubmed/?term=Venous+thromboembolism+in+heart+transplant+recipients%3A+incidence%2C+recurrence+and+predisposing+factors>.

- VTE is a frequent complication after HT, mainly during the first post-operative year. In view of a high recurrence rate, long-term anti-coagulation should be considered in HT recipients who experience a first VTE episode.

Martin ST, Kato TS, Farr M, et al. Similar survival in patients following heart transplantation receiving induction therapy using daclizumab vs. basiliximab. *Circ J*. 2015;79(2):368-74. doi: 10.1253/circj.CJ-14-0718. Epub 2014 Dec 12. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Similar+survival+in+patients+following+heart+transplantation+receiving+induction+therapy+using+daclizumab+vs.+basiliximab>.

- Survival following HTx was worse in patients not receiving induction therapy. No differences were noted in survival or the incidence of rejection between the daclizumab- and basiliximab-treated groups. Induction therapy was less used in patients with infection, which was related to prior VAD support.

Whitson BA, Kilic A, Lehman A, et al. Impact of induction immunosuppression on survival in heart transplant recipients: a contemporary analysis of agents. *Clin Transplant*. 2015 Jan;29(1):9-17. doi: 10.1111/ctr.12469. Epub 2014 Dec 12. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Impact+of+induction+immunosuppression+on+survival+in+heart+transplant+recipients%3A+a+contemporary+analysis+of+agents>.

- In a contemporary analysis of heart transplant recipients, an overall analysis of induction agents does not appear to impact survival, as compared to no induction immunosuppression. While ALG/ATG/thymoglobulin appeared to have a beneficial effect on survival compared to IL-2Rab in the univariable model, this difference was no longer statistically significant once we adjusted for clinically relevant covariates.

Chehrazi-Raffle A, Luu M, Yu Z, et al. Toxoplasma gondii Serology and Outcomes After Heart Transplantation: Contention in the Literature. *Transplant Proc*. 2015 Jul-Aug;47(6):1949-53. doi: 10.1016/j.transproceed.2015.06.022. Retrieved at:

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Toxoplasma+gondii+Serology+and+Outcomes+After+Heart+Transplantation%3A+Contention+in+the+Literature>.

- Toxoplasma serology prior to heart transplantation does not appear to impact post-transplantation outcome. However, toxoplasma seronegative patients who receive toxoplasma seropositive hearts appear to have poorer 5-year survival compared to toxoplasma seronegative patients who received toxoplasma seronegative hearts. Due to the small sample size, the association between T. gondii serology mismatch and long-term survival warrants further study.

Guihaire J¹, Noly PE¹, Martin A¹, Rojo M¹, Aymami M¹, Ingels A¹, Lelong B¹, Chabanne C¹, Verhoye JP¹, Flécher E¹. Impact of donor comorbidities on heart transplant outcomes in the modern era. *Interact Cardiovasc Thorac Surg*. 2017 Feb 20. doi: 10.1093/icvts/ivx014. [Epub ahead of print]. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28329066>

- The use of older cardiac donors with more cardiovascular comorbidities in the recent era did not impair the post-transplant outcomes. Donor hypertension was the only determinant of worse survival

Jahangirifard A¹, Razavi MR², Ahmadi ZH³, Forozeshfard M⁴. The Effect of Desmopressin on the Amount of Bleeding and Transfusion Requirements in Patients undergoing Heart Transplant Surgery. *Basic Clin Pharmacol Toxicol*. 2017 Mar 22. doi: 10.1111/bcpt.12780. [Epub ahead of print]. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28326680>

- Desmopressin may reduce postoperative bleeding in patients undergoing heart transplant surgery. Further studies are required to confirm the potential effect of desmopressin on establishing hemostasis following heart transplantation.

Kransdorf EP, Kittleson MM, Patel JK, Pando MJ, Steidley DE, Kobashigawa JA. Calculated panel-reactive antibody predicts outcomes on the heart transplant waiting list. *J Heart Lung Transplant*. 2017 Feb 17. pii: S1053-2498(17)31624-8. doi: 10.1016/j.healun.2017.02.015. [Epub ahead of print]. Retrieved from: [://www.ncbi.nlm.nih.gov/pubmed/28318744](https://www.ncbi.nlm.nih.gov/pubmed/28318744)

- Sensitized heart transplant candidates are at high risk of adverse outcomes on the heart transplant waiting list. Clinicians should strive to minimize the CPRA by maximizing specificity in the selection of HLA antigens to exclude. The optimal clinical approach for candidates with high CPRA requires further study.

Low ejection fraction in donor hearts is not directly associated with increased recipient mortality. Chen CW¹, Sprys MH², Gaffey AC¹, Chung JJ¹, Margulies KB³, Acker MA¹, Atluri P⁴. *J Heart Lung Transplant*. 2017 Feb 4. pii: S1053-2498(17)31348-7. doi: 10.1016/j.healun.2017.02.001. [Epub ahead of print]. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28314504>

- Recipients of hearts with reduced EF have equivalent 1-year survival compared with recipients of hearts with normal EF. Donor hearts with reduced EF show significant functional recovery after transplant.

Poglajen G¹, Jensterle M², Kravos N², Janež A², Vrtovec B¹ Low Serum Testosterone is Associated With Graft Function Early After Heart Transplantation. *Clin Transplant*. 2017 Mar 17. doi: 10.1111/ctr.12970. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28314079>

- Low serum testosterone levels appear to be associated with impaired graft function and an increased incidence of low-grade rejection episodes early after heart transplantation.

Bruminhent J^{1,2}, Cawcutt KA², Thongprayoon C³, Petterson TM⁴, Kremers WK^{4,5}, Razonable RR^{2,5}. Epidemiology, Risk Factors and Outcome of Clostridium difficile Infection in Heart and Heart-Lung Transplant Recipients. *Clin Transplant*. 2017 Mar 17. doi: 10.1111/ctr.12968. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28314071>

- CDI after HT is more common among patients with combined heart-lung and those undergoing retransplantation. CDI was associated with a higher risk of mortality in HT recipients.

Hasan R¹, Ela AA, Goldstein D. Innovations in cardiac transplantation. *Curr Opin Cardiol*. 2017 Mar 16. doi: 10.1097/HCO.0000000000000392. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28306670>

- This review highlights the most recent studies and future possible therapies that will improve outcomes in cardiac transplantation. Larger clinical trials are currently taking place and will be needed in the future to develop and sustain current trends toward better survival rates with cardiac transplantation.

Geft D¹, Kobashigawa J. Current concepts for sensitized patients before transplantation. *Curr Opin Organ Transplant*. 2017 Mar 16. doi: 10.1097/MOT.0000000000000411. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28306593>

- The development of more accurate methods of detecting sensitization and defining the ideal desensitization strategies that can be more universally adopted and tested in clinical trials will serve to enlighten us and help many more highly sensitized patients not only make it to transplant, but also thrive posttransplant as well.

Sabatino M¹, Vitale G², Manfredini V¹, Masetti M¹, Borgese L¹, Maria Raffa G², Loforte A¹, Martin Suarez S¹, Falletta C², Marinelli G¹, Clemenza F², Grigioni F¹, Potena L³. Clinical relevance of the International Society for Heart and Lung Transplantation consensus classification of primary graft dysfunction after heart transplantation: Epidemiology, risk factors, and outcomes. *J Heart Lung Transplant*. 2017 Feb 17. pii: S1053-2498(17)31623-6. doi: 10.1016/j.healun.2017.02.014. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28302502>

- Consensus-defined P-GD identifies patients at major risk for early death and graft loss after HT, although the "mild" grade appeared under-represented and clinically irrelevant. The amplified negative effect of donor and recipient factors on P-GD risk underscores the need for appropriate donor-recipient match.

Manfredini V¹, Leone O, Agostini V, Potena L. Antibody-mediated rejection in heart transplantation: new developments and old uncertainties. *Curr Opin Organ Transplant*. 2017 Mar 15. doi: 10.1097/MOT.0000000000000407. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28301387>

- Despite improvements in the diagnostic process, therapeutic strategies made little progress in addition to the consolidation of practices supported by limited evidences. Novel complement inhibitors appear promising in changing this scenario. Nevertheless, collaborative multicenter studies are needed to develop standardized approaches tailored to the highly variable clinical and laboratory features of AMR.

Hagiya H¹, Yoshida H¹, Yamamoto N¹, Kimura K², Ueda A², Nishi I², Akeda Y¹, Tomono K¹. Mycoplasma hominis periaortic abscess following heart-lung transplantation. *Transpl Infect Dis*. 2017 Mar 13. doi: 10.1111/tid.12697. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28294481>

- Report the first case of Mycoplasma hominis periaortic abscess after heart-lung transplantation

Benatti RD¹, Oliveira GH², Bacal F³. Heart Transplantation for Chagas Cardiomyopathy. *J Heart Lung Transplant*. 2017 Feb 3. pii: S1053-2498(17)31353-0. doi: 10.1016/j.healun.2017.02.006. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28284779>

- Chagas cardiomyopathy (CC) and heart transplantation review article

Sousa M¹, Monohan G¹, Rajagopalan N¹, Grigorian A¹, Guglin M². Heart transplantation in cardiac amyloidosis. *Heart Fail Rev*. 2017 Mar 9. doi: 10.1007/s10741-017-9601-z. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28281017>

- Cardiac amyloidosis and heart transplantation review article

Akiyama M¹, Takahara S², Kawatsu S², Endo Y³, Fujiwara J³, Adachi O², Kumagai K², Kawamoto S², Saiki Y². Successful management of antibody-mediated rejection after cardiac transplantation in a patient supported by a left ventricular assist device for more than 3 years. *Gen Thorac Cardiovasc Surg*. 2017 Feb 27. doi: 10.1007/s11748-017-0763-3. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28243893>

- Due to donor shortage, patients with refractory heart failure need to be supported on mechanical circulatory support (MCS). Critically, patients undergo several deployments of

MCS in stages inevitably requiring blood products transfusion. MCSs per se along with blood products can trigger immune allosensitization. Antibody-mediated rejection (AMR) is associated with significant mortality after heart transplantation. Here, we present the case with high panel-reactive antibody over 95% who developed AMR early after heart transplantation. This life-threatening complication was successfully treated with multi-modal treatment including anti-CD20 antibody, rituximab.

Erasmus M¹, Neyrink A, Sabatino M, Potena L. Heart allograft preservation: an arduous journey from the donor to the recipient. *Curr Opin Cardiol*. 2017 Feb 24. doi: 10.1097/HCO.0000000000000395. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28240643>

- The researches reviewed in this article support a significant improvement of the heart preservation during the multifaceted process of procurement, transport, and transplant. Future challenges will be to develop healing of currently unsuitable organs, while keeping the cost of technology within the borders of affordability for healthcare systems.

Jennings DL¹, Baker WL². Pre-cardiac transplant amiodarone use is not associated with postoperative mortality: An updated meta-analysis. *Int J Cardiol*. 2017 Feb 14. pii: S0167-5273(17)30236-X. doi: 10.1016/j.ijcard.2017.02.045. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28238350>

- Meta-analysis of the available evidence suggests that pre-operative amiodarone exposure does not increase mortality in cardiac transplant recipients.

Ruan V¹, Czer LS², Awad M¹, Kittleson M¹, Patel J¹, Arabia F³, Esmailian F³, Ramzy D³, Chung J³, De Robertis M³, Trento A³, Kobashigawa JA¹. Use of Anti-Thymocyte Globulin for Induction Therapy in Cardiac Transplantation: A Review. *Transplant Proc*. 2017 Mar;49(2):253-259. doi: 10.1016/j.transproceed.2016.11.034. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28219580>

- Use of Anti-thymocyte Globulin for induction therapy in cardiac transplant review article

Rakita RM¹, O'Brien KD², Bourassa L³. Diaporthe soft tissue infection in a heart transplant patient. *Transpl Infect Dis*. 2017 Feb 16. doi: 10.1111/tid.12680. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28207190>

- Infections caused by Diaporthe species are very uncommon. We describe a heart transplant recipient 14 years post transplant who developed a soft tissue fungal infection due to a Diaporthe species that responded well to surgical excision and posaconazole therapy. The

Aspergillus galactomannan index was markedly elevated, and returned to normal following treatment. Solid organ transplant patients remain at risk of infection long after transplant and should be counseled about risk avoidance.

Bürker BS^{1,2,3}, Gullestad L^{1,4}, Gude E⁴, Relbo Authen A⁴, Grov I⁴, Hol PK^{1,5}, Andreassen AK⁴, Arora S⁴, Dew MA⁶, Fiane AE^{1,7}, Haraldsen IR³, Malt UF^{1,2}, Andersson S⁸. Cognitive function after heart transplantation: Comparing everolimus-based and calcineurin inhibitor-based regimens. *Clin Transplant*. 2017 Feb 10. doi: 10.1111/ctr.12927. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28185318>

- Given the high prevalence of cognitive impairment in the sample, plus the known negative impact of cognitive impairment on clinical outcome, our results indicate that cognitive assessment should be an integrated part of routine clinical follow-up after HTx. However, everolimus- and CNI-based immunosuppressive regimens did not show differential impacts on cognitive function

Kransdorf EP¹, Loghmanpour NA², Kanwar MK³, Temkit MH⁴, Stehlik J⁵. Prediction model for cardiac allograft vasculopathy: Comparison of three multivariable methods. *Clin Transplant*. 2017 Feb 9. doi: 10.1111/ctr.12925. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28181298>

- We have developed a clinical prediction model for assessing a recipient's risk of CAV using variables available at the time of HT. Application of this model may allow clinicians to determine which recipients will benefit from interventions to reduce the risk of development and progression of CAV.

Elboudwarej O¹, Phan D¹, Patel JK¹, Liou F¹, Aintablian T¹, Osborne A¹, Yu Z¹, Reinsmoen N¹, Kobashigawa JA¹. Corticosteroid wean after heart transplantation-Is there a risk for antibody formation? *Clin Transplant*. 2017 Jan 30. doi: 10.1111/ctr.12916. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28135788>

- Few patients successfully weaned off prednisone after heart transplant develop de novo circulating antibodies but are not at increased risk for developing rejection.

Shudo Y1, Hiesinger W1, Oyer PE1, Woo YJ1. Operative technique and pitfalls in donor heart procurement. *Asian Cardiovasc Thorac Ann*. 2017 Jan;25(1):80-82. doi:

10.1177/0218492316678716. Epub 2016 Nov 12. Retrieved from:
<https://www.ncbi.nlm.nih.gov/pubmed/28074702>

- We describe a simple and reproducible donor heart procurement technique in sequential steps. A detailed understanding of procurement and organ preservation techniques should be an essential part of a heart transplant training program.

Rossano JW¹, Jefferies JL², Pahl E³, Naftel DC⁴, Pruitt E⁴, Lupton K⁵, Dreyer WJ⁶, Chinnock R⁷, Boyle G⁸, Mahle WT⁹; Pediatric Heart Transplant Study Investigators. Use of sirolimus in pediatric heart transplant patients: A multi-institutional study from the Pediatric Heart Transplant Study Group. *J Heart Lung Transplant*. 2017 Apr;36(4):427-433. doi: 10.1016/j.healun.2016.09.009. Epub 2016 Oct 4. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/28029575>

- Sirolimus was used in less than 10% of patients at 1 year post-transplant. Overall outcomes of sirolimus treated and non-treated patients were similar with respect to survival and major transplant adverse events. Further study of sirolimus in pediatric heart transplant patients is needed.

Simha V¹, Qin S², Shah P¹, Smith BH³, Kremers WK³, Kushwaha S⁴, Wang L⁵, Pereira NL^{6,7}. Sirolimus Therapy Is Associated with Elevation in Circulating PCSK9 Levels in Cardiac Transplant Patients. *J Cardiovasc Transl Res*. 2017 Feb;10(1):9-15. doi: 10.1007/s12265-016-9719-8. Epub 2016 Dec 27.

- Sirolimus used in transplantation is often associated with hypercholesterolemia. We measured serum lipid and PCSK9 levels in 51 heart transplant recipients who had their immunosuppressive therapy switched from calcineurin inhibitors to sirolimus. The switch resulted in a 23% increase in LDL cholesterol, and 46% increase in triglycerides and PCSK9 levels increased from 316 ± 105 ng/mL to 343 ± 107 ng/mL ($p = 0.04$), however the change in PCSK9 levels did not correlate with an increase in lipid levels ($p = 0.2$). To investigate the mechanism for the variability in the change in PCSK9 levels, lymphoblastoid cell lines were incubated with both sirolimus and everolimus, resulting in a 2-3 fold increase in PCSK9 expression and protein levels in mTOR inhibitor sensitive but not in mTOR inhibitor resistant cell lines. This first in human study demonstrates that sirolimus therapy is associated with elevation in PCSK9 levels which is not associated with sirolimus-induced hypercholesterolemia.

Fahrleitner-Pammer A¹, Wagner D², Krisper P³, Amrein K⁴, Dimai H⁴. Teriparatide treatment in a heart transplant patient with a chronic kidney disease and a low-turnover bone disease: a case report. *Osteoporos Int.* 2017 Mar;28(3):1149-1152. doi: 10.1007/s00198-016-3858-2. Epub 2016 Dec 17. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27988794>

- Low-turnover bone disease is a complication of chronic kidney disease and a long-term steroid therapy. Currently, the only bone anabolic treatment available is teriparatide (TPTD). So far, no data exist in heart transplant patients, and only one single case with histomorphometric analysis of a dialysis patient with a low-turnover bone disease has been published. The current report shows the effect of a 1-year TPTD therapy in a cardiac transplant patient with 10 vertebral and 3 peripheral fractures who had developed a chronic kidney failure while receiving triple immunosuppressive therapy. A transiliac bone biopsy following tetracycline labeling was performed prior and after 1 year of treatment, showing an increase in the bone formation and improvement of the structural indices (20-fold increase of osteoid volume/bone volume, fourfold increase of osteoid surface/bone surface and increases of wall thickness (+15%), trabecular thickness (+9%), and trabecular number (+38%)). Bone mineral density was stable, no new vertebral fractures had occurred, the therapy was well-tolerated, and the patient improved clinically.

Echenique IA¹, Angarone MP¹, Gordon RA², Rich J², Anderson AS², McGee EC³, Abicht TO³, Kang J⁴, Stosor V^{1,5}. Invasive fungal infection after heart transplantation: A 7-year, single-center experience. *Transpl Infect Dis.* 2017 Feb;19(1). doi: 10.1111/tid.12650. Epub 2017 Jan 27. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27943503>

- The cumulative incidence was 10.7%. IFIs were associated with pre- and post-HT vancomycin-resistant *Enterococcus* colonization and/or infection, post-HT renal replacement therapy, anti-thymocyte globulin induction, and antibody-mediated rejection. There were no associations with diabetes mellitus, desensitization, 2R/3R cellular rejection, treatments for rejection, re-operation, neutropenia, or cytomegalovirus infection. IFIs were associated with death (P=.02, OR 3.9, 95% CI 1.3-12.1) and 1-year mortality (P<.001, OR 9.0, 95% CI 2.3-35.7), but not 3-year mortality. Associations with Hispanic ethnicity must be validated. Optimal strategies for risk reduction and prophylaxis remain undefined.

Arman D¹, Kuraitis D¹, Moriguchi J¹, Hamilton M¹, Liou F¹, Siddiqui S¹, Luu M¹, Zakowski P², Arabia F¹, Kobashigawa J³. Do Prior Driveline Infections Increase the Risk of Infection in Heart Transplant Patients Treated With Rabbit Antithymocyte Globulin Induction Therapy? *Transplant Proc.* 2016 Dec;48(10):3393-3396. doi: 10.1016/j.transproceed.2016.09.037. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27931587>

- The use of ATG induction in patients with prior DLIs did not seem to increase the risk for posttransplant infection (eg, sternal wound infection). ATG induction can therefore be safely used in this population.

Furiasse N¹, Kobashigawa JA¹. Immunosuppression and adult heart transplantation: emerging therapies and opportunities. *Expert Rev Cardiovasc Ther.* 2017 Jan;15(1):59-69. Epub 2016 Dec 14. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27918214>

- Immunosuppression following heart transplantation has improved graft longevity through the reduction of cellular and antibody mediated rejection. The attempt to limit the unintended consequences of immunosuppressive therapies and address sensitized patients has led to a revolution in immunosuppression. Areas covered: This review will focus on the current emerging immunosuppressive therapies in heart transplantation while reviewing the effective contemporary treatments, and explore the potential development of new immunomodulatory therapies. An exhaustive review of the PubMed database and abstract data from national meetings was performed to compile the data for the manuscript. Expert commentary: The timing and targets of immunosuppressive therapies are evolving to provide adjunctive therapies to the established treatments. Recent advances will allow for further tailoring of immunomodulatory therapies to the individual patient

Clerkin KJ¹, Farr MA¹, Restaino SW¹, Zorn E², Latif F¹, Vasilescu ER³, Marboe CC³, Colombo PC¹, Mancini DM⁴. Donor-specific anti-HLA antibodies with antibody-mediated rejection and long-term outcomes following heart transplantation.

J Heart Lung Transplant. 2016 Nov 17. pii: S1053-2498(16)30403-X. doi: 10.1016/j.healun.2016.10.016. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27916323>

- DSA were inadequate to diagnose pAMR. Class II DSA provided prognostic information regarding future pAMR, graft dysfunction with pAMR, and graft loss

Bennett AL¹, Ventura HO². Hypertension in Patients with Cardiac Transplantation. *Med Clin North Am.* 2017 Jan;101(1):53-64. doi: 10.1016/j.mcna.2016.08.011. Epub 2016 Oct 27. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27884235>

- Hypertension is a common complication among post cardiac transplant recipients affecting more than 95% of patients. Increased blood pressure poses a significant cardiovascular morbidity and mortality in these patients; it should be identified quickly and needs to be

managed appropriately. Understanding the pathophysiology and contributing factors to this disease in these complex and unique patients is the key to appropriate treatment selection

Lushaj EB¹, Dhingra R², Chindhy S¹, Akhter S¹, Kohmoto T¹, Ulschmid S¹, Osaki S¹, Badami A¹, Lozonschi L³. To use or not to use? Amiodarone before heart transplantation. *Surgery*. 2016 Nov 19. pii: S0039-6060(16)30620-1. doi: 10.1016/j.surg.2016.09.034. [Epub ahead of print] Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27876282>

- Amiodarone use did not affect the incidence of atrial fibrillation nor 30-day and 1-year survival post-transplantation. Nevertheless, post-transplant pulmonary complications were significantly greater and 5-year survival was less among patients treated with amiodarone prior to transplant

Das B¹, Dimas V¹, Guleserian K², Lacelle C³, Anton K⁴, Moore L⁴, Morrow R⁴. Alemtuzumab (Campath-1H) therapy for refractory rejections in pediatric heart transplant recipients. *Pediatr Transplant*. 2017 Feb;21(1). doi: 10.1111/petr.12844. Epub 2016 Nov 11. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27862703>

- Despite substantial improvements in survival after pediatric heart transplantation, refractory rejection remains a major cause of morbidity and mortality. We have utilized ALE (Campath-1H) in six consecutive patients with refractory rejection. These rejection episodes persisted despite conventional treatment, which included intravenous methylprednisolone, rituximab, immunoglobulin G, and antithymocyte globulin. In our series, after ALE therapy, LV SF increased from 22%±5% to 33%±5% (P=.01). However, in our series, ALE therapy neither led to persistent LV function recovery nor could it prevent subsequent antibody-mediated rejection

Mehra MR¹. *JAMA Cardiol*. 2017 Jan 1;2(1):98-99. doi: 10.1001/jamacardio.2016.3756. Guidelines for Listing Candidates for Heart Transplant: A 10-Year Update. *JAMA Cardiol*. 2017 Jan 1;2(1):98-99. doi: 10.1001/jamacardio.2016.3756. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27806174>

Cajita MI¹, Denhaerynck K², Dobbels F³, Berben L², Russell CL⁴, Davidson PM¹, De Geest S⁵; BRIGHT study team. Health literacy in heart transplantation: Prevalence, correlates and associations with health behaviors-Findings from the international BRIGHT study. *J Heart Lung Transplant*. 2017 Mar;36(3):272-279. doi: 10.1016/j.healun.2016.08.024. Epub 2016 Sep 13. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27773449>

- Clinicians should recognize that almost one third of heart transplant participants have inadequate health literacy. Furthermore, they should adopt communication strategies that could mitigate the potential negative impact of inadequate HL.

Ducharme-Smith A¹, Katz BZ², Bobrowski AE², Backer CL², Pahl E². BK polyomavirus infection in pediatric heart transplant recipients: a prospective study. *Pediatr Transplant*. 2017 Mar;21(2). doi: 10.1111/petr.12830. Epub 2016 Oct 20. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27762478>

- BKV infection and nephropathy complicate pediatric HTx, but the incidence and time course of the disease are unknown. We assessed the incidence of BKV infection and its association with kidney dysfunction in pediatric HTx recipients. A single center prospective study compared pediatric (<18 years) HTx recipients, with and without BKV infection, who received an allograft between September 2013 and December 2014. Screening of urine for BKV was performed prior to transplant, and at week 1, and at months 3, 6, 9, 12, and 15 months post-transplantation. Serum for BKV DNA was assayed if BK viruria was present. Statistics included Fisher's exact test and Student's t test. Twelve patients were enrolled. Two patients were removed per parent request. Two (20%) had BK viruria and one (10%) had BK viremia. No patients developed BKVN. BK viruria was present within 2 months following transplantation. There were no identifiable risk factors for BKV infection and no statistically significant difference in renal function between the groups; however, there was a trend toward worsening renal function in those with BKV infection. BKV infection can occur early following heart transplantation. Screening for BK viruria should be considered in HTx recipients

Ciarka A¹, Lund LH², Van Cleemput J³, Voros G³, Droogne W³, Vanhaecke J³. Effect of Heart Rate and Use of Beta Blockers on Mortality After Heart Transplantation. *Am J Cardiol*. 2016 Dec 15;118(12):1916-1921. doi: 10.1016/j.amjcard.2016.08.084. Epub 2016 Sep 15. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27743576>

- Heart transplantation (HT) recipients may have tachycardia secondary to cardiac denervation. As higher heart rate predicts worse outcomes in cardiovascular disease, we hypothesized that tachycardia and nonuse of β blockers are associated with increased mortality after HT. All patients who underwent HT at our institution from 1987 to 2010 were included. The association of heart rate 3 months after HT and β -blocker use during follow-up to mortality was assessed using Kaplan-Meier and multivariate Cox proportional hazards regression analyses adjusting for clinically relevant baseline variables. From 1987 to 2010, there were 493 HT. After excluding 29 who died within 3 months and 3 with follow-up <3 months, 461 HT recipients (50 \pm 2 years; 20% women) were included. Over a follow-up of 12 \pm 7 years, selected important univariate predictors of post-HT mortality were older age, male gender, higher body mass index, ischemic cardiomyopathy, longer post-HT intensive care unit stay, and hospitalization and at 3 months, increased mean pulmonary artery pressure, right atrial pressure and pulmonary capillary occlusion pressure, higher heart rate, and nonuse of β blockers during follow-up. In multivariate analysis, older age, longer hospitalization, higher mean pulmonary artery pressure, higher heart rate at 3 months (hazard ratio 1.02 per beat, 95% confidence interval 1.008 to 1.035,

p = 0.02) and nonuse of β blockers (hazard ratio 1.43, 95% confidence interval 1.002 to 2.031, p <0.05) were associated with mortality. In conclusion, in a large single-center cohort of HT recipients, higher heart rate and nonuse of β blockers were independently associated with higher mortality.

Stepanova M^{1,2}, Locklear T³, Rafiq N^{1,3}, Mishra A^{1,3}, Venkatesan C³, Younossi ZM^{1,3}. Long-term outcomes of heart transplant recipients with hepatitis C positivity: the data from the U.S. transplant registry. *Clin Transplant*. 2016 Dec;30(12):1570-1577. doi: 10.1111/ctr.12859. Epub 2016 Nov 8. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27739127>

- Chronic hepatitis C infection is associated with a significantly increased post-transplant mortality in heart transplant recipients. The introduction of new direct-acting antiviral agents may provide a treatment option for HCV pre- or post-heart transplantation which could have a positive impact on patients' survival.

Cooper LB^{1,2}, Milano CA^{3,4}, Williams M⁴, Swafford W⁴, Croezen D⁵, Van Bakel AB⁶, Rogers JG^{2,3}, Patel CB^{2,3}. Thyroid hormone use during cardiac transplant organ procurement. *Clin Transplant*. 2016 Dec;30(12):1578-1583. doi: 10.1111/ctr.12860. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27726211>

- Thyroid hormone use can have important implications for organ selection and cardiac function before and after transplantation. Protocols vary widely with respect to why and how to use and wean thyroid hormone. We believe there should be more detailed reporting of thyroid hormone use for future studies to ensure appropriate donor management.

Bradley D¹, Moreira S, Subramoney V, Chin C, Ives J, Wang K; Valcyte NP22523 Study Team. Pharmacokinetics and Safety of Valganciclovir in Pediatric Heart Transplant Recipients 4 Months of Age and Younger. *Pediatr Infect Dis J*. 2016 Dec;35(12):1324-1328. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27580058>

- The pediatric dosing algorithm for VGCV (utilizing individuals' body surface area and renal function) provides systemic GCV exposures in patients younger than 4 months that are similar to those observed in older pediatric populations. The data indicate that this dosing algorithm is appropriate across the entire pediatric age range, including this youngest age group.

Cooper LB¹, Mentz RJ², Edwards LB³, Wilk AR³, Rogers JG², Patel CB², Milano CA⁴, Hernandez AF², Stehlik J⁵, Lund LH⁶. Amiodarone use in patients listed for heart transplant is associated with increased 1-year post-transplant mortality. *J Heart Lung Transplant*. 2017 Feb;36(2):202-210. doi: 10.1016/j.healun.2016.07.009. Epub 2016 Jul 17. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27520780>

- Amiodarone use before OHT was independently associated with increased 1-year mortality. The need for amiodarone therapy should be carefully and continuously assessed in patients awaiting OHT

Roman DD¹, Holker EG¹, Missov E², Colvin MM³, Menk J⁴. Neuropsychological functioning in heart transplant candidates. *Clin Neuropsychol*. 2017 Jan;31(1):118-137. doi: 10.1080/13854046.2016.1212096. Epub 2016 Aug 5. Retrieved from: <https://www.ncbi.nlm.nih.gov/pubmed/27491277>

- End stage heart disease/heart failure is associated with global, mild to moderate cognitive impairment, regardless of age or neurological co-morbidities. Contributing factors likely include cerebrovascular hypoperfusion, multiorgan failure, systemic co-morbidities, and lifestyle issues.