TURIN, 20TH—21ST NOVEMBER 2008

GREAT INNOVATIONS IN CARDIOLOGY

4TH JOINT MEETING WITH MAYO CLINIC

4TH TURIN CARDIOVASCULAR NURSING CONVENTION

GESTIONE POST TRAPIANTO

D. Pasero (Torino), M. Brancalion (Torino)

In rianimazione

Daniela Pasero, MD
Department of Anaesthesiology
University of Turin

ICU management of cardiac transplant patient

ICU stay

2006: 25 Heart transplantation

ICU LOS > 48 h : 13/25 (52%)

ICU LOS, median (days): 4 (2 – 70)

Time to extubation: median 45h (16h - 36 days)

ICU Mortality : 5/25 (20%)

Epidemiology

Registry of the International Society for Heart and Lung Transplantation: Twenty-fifth Official Adult Heart Transplant Report—2008

David O. Taylor, MD, Leah B. Edwards, PhD, Paul Aurora, PhD, MRCP, Jason D. Christie, MD, MS, Fabienne Dobbels, PhD, Richard Kirk, MA, FRCP, FRCPH, Axel O. Rahmel, MD, Anna Y. Kucheryavaya, MS, and Marshall I. Hertz, MD

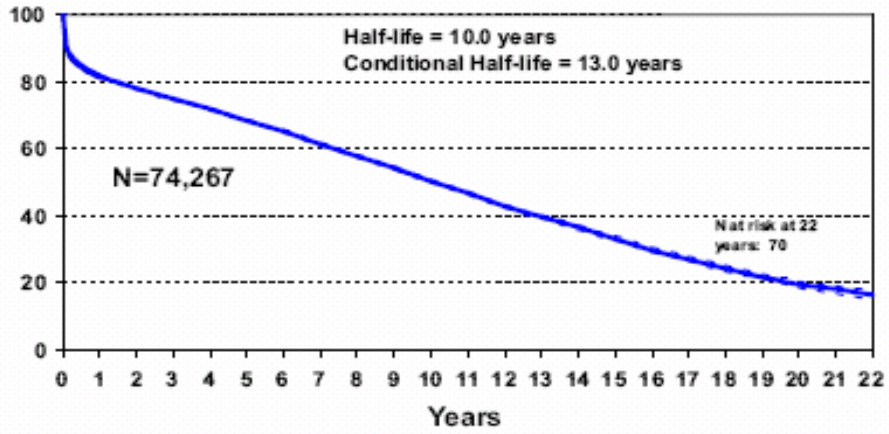

Figure 7. Kaplan–Meier survival for adult and pediatric heart transplants performed between January 1982 and June 2006. Conditional half-life = time to 50% survival for those recipients surviving the first year post-transplantation.

The Journal of Heart and Lung Transplantation
September 2008

Registry of the International Society for Heart and Lung Transplantation: Twenty-fifth Official Adult Heart Transplant Report—2008

David O. Taylor, MD, Leah B. Edwards, PhD, Paul Aurora, PhD, MRCP, Jason D. Christie, MD, MS, Fabienne Dobbels, PhD, Richard Kirk, MA, FRCP, FRCPH, Axel O. Rahmel, MD, Anna Y. Kucheryavaya, MS, and Marshall I. Hertz, MD

Table 2. Risk Factors for Mortality Within 1 Year for Transplants Performed January 2002 Through June 2006 (N = 8,823)

Variable	*N*	Relative risk	*p*-value	95% confidence interval
Temporary circulatory support[a]	137	3.19	<0.0001	2.32–4.37
Diagnosis: congenital vs cardiomyopathy	228	1.89	0.0002	1.35–2.64
Recipient on ventilator at time of transplant	248	1.50	0.0044	1.13–1.98
Recipient history of dialysis	273	1.48	0.0021	1.15–1.91
Recipient with infection requiring intravenous drug therapy within 2 weeks prior to transplant	923	1.30	0.0047	1.08–1.56
Long-term pulsatile device	1,456	1.26	0.0205	1.04–1.53
Not ABO-identical	1,288	1.25	0.0067	1.06–1.46
Prior transfusion	1,749	1.19	0.0432	1.01–1.41
Diagnosis: coronary artery disease vs cardiomyopathy	3,939	1.16	0.0431	1.00–1.35
Recipient on inotropes at time of transplant	3,673	0.85	0.0282	0.73–0.98
Recipient age (J-shaped)			<0.0001	
Recipient height (inverse linear)			<0.0001	
Donor age (curvilinear)			<0.0001	
Donor BMI (inverse linear)			0.0288	
Transplant center volume (inverse linear)			0.0032	
Ischemia time (linear)			0.0060	
Pulmonary artery diastolic pressure (linear)			0.0004	
Serum bilirubin (linear)			0.0006	
Serum creatinine (linear)			0.0001	

Therapeutic goals

- Hemodynamic: HR 90-110 bpm

  PVC 12-16 mmHg

  PW 14-18 mmHg

  MAP >65 mmHg

- Early extubation
- Prophylaxis of infections
- Immunosuppression

Complications

- Right ventricular dysfunction
- Left ventricular dysfunction
- Coagulation
- Renal dysfunction
- Pulmonary dysfunction
- Hyperacute allograft rejection
- Infections

Autonomic denervation

Transection of the autonomic plexus

- no response to direct ANS stimulation

- no response to drugs acting throught ANS (atropine)

- response to catecholamines

Transient slow nodal rythms after CBP are common

- inotropes:

Isoproterenol: chronotropic, inotropic vasodilator.

Dopamine, dobutamine, epinephrine

- pacing (5-10% permanent PM)

Right ventricular dysfunction

Significant cause of early morbidity and mortality (20% early deaths)

Etiology

- Preexistent pulmonary HTN (TPG > 12-15 mmHg)
- Transient pulmonary vasospasm
- IT o IP secondary to early post-operative RV dilation
- Donor-recipient size mismatch
- Prolonged donor heart ischemic time, Inadeguate myocardial protection, surgical manipulation

Diagnosis

- TEE, Tricuspidal regurgitation
- Surgical field
- ↑ PVC, PAP, TPG (> 15 mmHg)

Right ventricular dysfunction

Therapeutic goals:

Decrease PVR

- PVR < 6 WU TPG < 5-10 mmHg
- Increase FiO2, Correction acid-base abnormalities
- Hyperventilation (PaCO2 25-30 mmHg)
- Pulmonary vasodilation: nitrates, prostacyclin (PGI2), prostaglandin E1 (PGE1), Phosphodiesterase III inhibitors, inhaled NO

Improve RV function

- Inotropic support

Right ventricular dysfunction

Inhaled Nitric Oxide

Cardiac surgery

Heart transplantation

Several institutions with extensive experience in cardiac transplantation use and recommend iNO as a part of standard therapy for all cardiac transplant procedures associated with increased PVR

Germann P et al. Intensive Care Med 2005; 31: 1029-1041

Left ventricular dysfunction

- Prolonged high dose inotropic support before organ harvest
- Inadequate myocardial perfusion
- Prolonged donor heart ischemic time
- Intracoronary air embolization
- Surgical manipulation

Monitoring, inotropes, IABP, VAD.

Renal dysfunction

Etiology

Pre-existing renal impairment

Cyclosporine associated renal toxicity

Perioperative low cardiac output states

CBP (Ht, T°)

Treatment

Optimization CO and systemic BP

Diuretics

Dose adjustment or substitution of nephrotoxic drugs

CVVH (avoid fluid overload)

Pulmonary dysfunction

Etiology

Atelectasis

Pleural effusion

Pneumonia

Congestion

Pulmonary HTN

Treatment

OLV , Physiotherapy, Regular endobronchial suctioning

Inotropes, diuretics

Early and aggressive treatment of infections

Immunosuppression

Induction Therapy With Thymoglobulin After Heart Transplantation: Impact of Therapy Duration on Lymphocyte Depletion and Recovery, Rejection, and Cytomegalovirus Infection Rates

Sorel Goland, MD, Lawrence S. C. Czer, MD, Bernice Coleman, PhD, Michele A. De Robertis, RN, James Mirocha, MS, Kaveh Zivari, BS, Ernst R. Schwarz, MD, PhD, Robert M. Kass, MD, and Alfredo Trento, MD

Both Thymoglobulin regimens were well tolerated. The 7-day treatment led to more efficient and prolonged lymphocyte depletion and significantly less rejection at 1 year, without an increase in cytomegalovirus infection rate. J Heart Lung Transplant 2008;27:1115-21.

The Journal of Heart and Lung Transplantation
October 2008

pression. The triple therapy consists of steroids (prednisone), calcineurin inhibitor (CNI; cyclosporine or tacrolimus), and an antiproliferative agent (azathioprine or mycophenolate mofetil). Because of the significant side effects of steroids, many cardiac transplant programs tend to maintain recipients on double-drug therapy with a CNI and an antiproliferative agent. There are two general approaches to

Annu. Rev. Med. 2006. 57:455–71

Immunosuppression

New Directions in Cardiac Transplantation

Abdulaziz Al-khaldi and Robert C. Robbins
Department of Cardiothoracic Surgery, Stanford University School of Medicine, Stanford, California; email: alkhaldi@stanford.edu, robbins@stanford.edu

TABLE 1 Steroid-free immunosuppression protocols in cardiac transplantation

Protocol (references)	Description	Success rate
Early withdrawal (90–93)	Steroid withdrawal during the first month after transplant	48%–70%
Late withdrawal (94–97)	Steroid withdrawal after the first 6 months post-transplant (the period of highest risk of rejection)	~80%

Annu. Rev. Med. 2006. 57:455–71

Immunosuppression

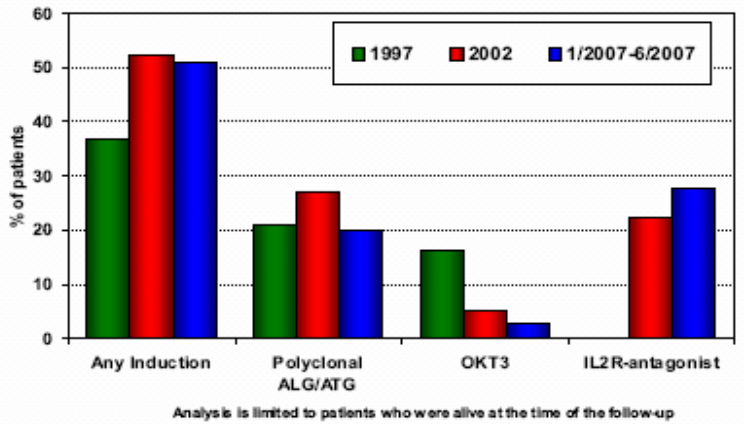

Figure 3. Anti-lymphocyte antibody use for induction immunosuppression by year of heart transplant as performed in 1997, 2002 and January to June 2007. ATG, anti-thymocyte globulin; ALG, anti-lymphocyte globulin; IL-2R, interleukin-2 receptor.

Induction Immunosuppression

Maintenance Immunosuppression

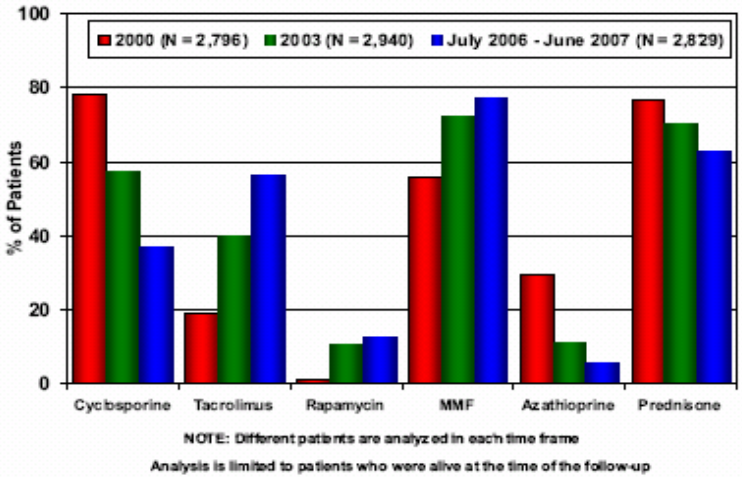

Figure 4. Maintenance immunosuppressive agents at 1-year post-transplantation follow-up 2000, 2003 and July 2006 to June 2007. MMF, mycophenolate mofetil; AZA, azathioprine; Rapa, rapamycin.

Immunosuppression

	Thymoglobulin	Steroids	Cyclosporine	Mycophenolate
OR	1.25-2.5 mg/kg/day For 3-10 days	Metihylprednisolone 1000 mg IV in OR		
ICU		Metihylprednisolone 125 mg IV q8h	2mg/k/day IV	1 g PO bid
		Prednisone 0,5 mg/kg PO bid	3mg/kg PO bid	
		Prednisone 0,5 mg/kg PO bid		
		Decrease total daily dose by 10 mg		
		Qd until 30 mg qd is reached		

Hyperacute allograft rejection

Abstract

The terminology of hyperacute rejection (HAR) has become outmoded and confusing due both to advances that have been made in delaying its onset and due to a proliferation of synonyms for the same pathologic process. Until such time as antibody-mediated xenograft rejection can be classified by the type of causative antibody, it is recommended that the term hyperacute rejection be applied to antibody-mediated rejection with *classical HAR* occurring within 24 h. *Delayed HAR* is the same pathologic process encountered after 24 h. Recognition of the key role that venous thrombosis plays in the pathogenesis of HAR allows the microscopist to intelligently interpret biopsies from various portions of a transplanted organ according to the pathologic effects of the obstructed venous drainage of the organ. Particularly in the heart, HAR often shows different pathologic features in the inner compared to the outer myocardium. Once xenografting becomes feasible, it will be possible to apply a grading system of HAR in clinical practice.

- Rare
- Severe cardiac dysfunction and death within hours of transplantation
- Assisted mechanical support until cardiac re-transplantation

Cardiovascular Pathology 11 (2002) 171–176

Coagulation

Causes

- hepatic dysfunction (chronic hepatic venous congestion)
- pre-operative anticoagulation
- CBP: PLT dysfunction , hypothermia, hemodilution of clotting factors

Treatment

- Mediastinal re-exploration (increased morbidity)
- Blood products CMV negative, irradiated, leukocyte depleted (infection, GVHD)
- Leukocyte filters

Infections

- High risk in the early postoperative period (high-dose immunosuppression)
- Wash hands (no isolation required)
- 48-hour course of perioperative prophylactic ATB

Infections: CMV

High Incidence of Cytomegalovirus Disease in D^+/R^- Heart Transplant Recipients Shortly After Completion of 3 Months of Valganciclovir Prophylaxis

Sachin Gupta, MD,[a] Joshua D. Mitchell, BS,[a] David W. Markham, MD,[a] Pradeep P. A. Mammen, MD,[a] Parag C. Patel, MD,[a] Patricia Kaiser, RN,[b] W. Steves Ring, MD,[c] J. Michael DiMaio, MD,[c] and Mark H. Drazner, MD, MSc[a]

CMV: in all recipients use leukodepleted blood

R-/D-: no prophylaxis

R or D positive: Ganciclovir 5mg/kg /day for 14 days, starting on day 2, then Vanganciclovir 450 mg bid, for three months.

R-/D+: add Ig IV 150 mg /kg at 72 h, at 2 weeks, 4 weeks, 6 weeks, 8 weeks and 100 mg/kg at 12 and 16 weeks after the transplantation

The Journal of Heart and Lung Transplantation
Volume 27, Number 5 2008

Infections

- Toxoplasma:

  R-/D+: pyrimethamine 25 mg qd and folinic acid 6 mg qd for 6 weeks

scribed after cardiac transplantation where, in the absence of prophylaxis, *Toxoplasma*-seronegative recipients of a seropositive heart (donor-recipient mismatch [DRMM]) experience a 50% to 75% risk of symptomatic infection. This may present as myocarditis, brain abscess, or disseminated disease

Conclusions. We therefore conclude that in transplant centers with low *Toxoplasma* seroprevalence, routine screening for *Toxoplasma* in solid organ donors and recipients is not necessary, particularly in the era of routine TMP/SMX prophylaxis.

Transplantation 2008;85: 980–985

Is Toxoplasmosis Prophylaxis Necessary in Cardiac Transplantation? Long-term Follow-up at Two Transplant Centers

David A. Baran, MD,[a] Mamata M. Alwarshetty, MD,[a] Saad Alvi, MD,[a] Luis H. Arroyo, MD,[a] Steven Lubitz, MD,[b] Sean Pinney, MD,[b] Alan L. Gass, MD,[b] and Mark J. Zucker, MD[a]

Cardiac transplant recipients are often given prophylactic treatments to prevent opportunistic infections such as *Pneumocystis carinii*. Toxoplasmosis prophylaxis is commonly prescribed for transplant recipients who have not been exposed to this disease but receive a heart from an exposed donor. We reviewed the collective 28-year experience at two urban transplant programs with 596 patients, and found no cases of toxoplasmosis, but all patients received trimethoprim–sulfamethoxazole to prevent *Pneumocystis* pneumonia. We conclude that specific anti-toxoplasmosis prophylaxis is unnecessary in heart transplant recipients. J Heart Lung Transplant 2006;25:1380–2.

The Journal of Heart and Lung Transplantation
Volume 25, Number 11

- Pneumocystis Carinii: sulfamethoxazole-trimethoprim 1 tablet PO bid 3 times/week for 1 year.

Conclusion

Cardiac transplantation continues to be the gold standard for the treatment of end-stage cardiac diseases refractory to medical therapy. Survival after HTx has improved with each era, probably owing to the better selection of donors and recipients as well as the development of more selective and effective immunosuppression agents. In the future, the widespread use of VADs for destination therapy and further improvement of medical therapy will permit the genetic allocation of donor hearts to the most nearly ideal group of heart failure patients (about 2000–2500 patients in the United States), and that will further increase post-transplantation survival.

Annu. Rev. Med. 2006. 57:455–71