Journal of Clinical Nephrology & Kidney Diseases

Research Article
Published: 18 Apr, 2017

Long Term Graft and Recipient Outcome of Deceased Donor Renal Transplantation at the National Kidney and Transplant Institute

*Tam MJC, Cabanayan-Casasola CB and Danguilan RA**

Department of Adult Nephrology, National Kidney and Transplant Institute, East Avenue, Quezon City, Philippines

Abstract

Background: The number of patients with ESRD is increasing and the gap between the demand for KT and available donors is widening. Thus deceased donation is very important to the donor pool for ESRD.

Objectives: This study aims to determine the long term graft and recipient outcome of deceased donor renal transplantation at the National Kidney and Transplant Institute from 2002-2007 and to determine the donor and recipient factors that affect graft and recipient survival.

Materials and Methods: This is a retrospective cohort of deceased donor KT from January 2002 to December 2007. Data were reviewed and collected from National Kidney and Transplant Institute medical records and the Philippine Renal Disease Registry (PRDR). Recipient and donor demographic profile were expressed as frequency counts, percentages and means with standard deviation. Kaplan Meier was used to determine graft and patient survival and logistic regression to establish correlation between certain factors and survival.

Results: Among 1,598 KT, 1,488 were from living donors and 110 from deceased donors. In the study, 91 patients were included. The mean recipient age was 40.40 ± 11.8 years and 65.9% were males. The primary renal diseases were chronic glomerulonephritis (63.7%), diabetic nephropathy (18.7%) and hypertensive nephrosclerosis (6.6%). Around 39.6% had 3 HLA mismatches and 61.5% had at least 1 DR match. Majority received induction therapy (90.1%) and 64.8% had tacrolimus based immunosuppressive regimen. The patient survival rate at 1st, 3rd, 5th and 7th years was 91%, 89%, 86% and 86% while graft survival was 89%, 79%, 73% and 68% respectively. Infection was the leading cause of death. Cold ischemia time was significantly associated with patient survival (P=0.033) while patients with male donors had significantly better graft survival (P=0.001).

Conclusion: There was an acceptable outcome of KT from deceased donors up to 7 years post KT.

Keywords: Cadaveric donor kidney transplantation; Graft survival; Patient survival

OPEN ACCESS

Correspondence:
Danguilan RA, Department of Adult Nephrology, National Kidney and Transplant Institute, East Avenue, Quezon City, Philippines, Tel: 639175224354;
E-mail: dr.radanguilan@gmail.com

Received Date: *27 Feb 2017*
Accepted Date: *13 Apr 2017*
Published Date: *18 Apr 2017*

Citation:
Tam MJC, Cabanayan-Casasola CB, Danguilan RA. Long Term Graft and Recipient Outcome of Deceased Donor Renal Transplantation at the National Kidney and Transplant Institute. J Clin Nephrol Kidney Dis. 2017; 2(1): 1009.

Introduction

Kidney transplantation (KT) is the preferred treatment for end stage renal disease (ESRD). A successful transplant triples the life expectancy of a renal failure patient. The projected life expectancy with a transplant was 17.19 years compared with only 5.84 years on dialysis [1]. Hence, despite an initial higher risk of death, long-term survival for patients who underwent transplantation is significantly better compared with patients who remain on dialysis.

In addition, KT is more cost effective and improves quality of life. A study showed that the costs of patient therapy by hemodialysis are far greater than transplantation and its maintenance by almost three and a half times [2]. In a study [3], composed of 50 kidney transplant patients and 100 hemodialysis patients which measured the quality of life using the validated McGill Questionnaire consisting of a part A (total life quality: physical, emotional, social, spiritual and financial) and 16 questions divided in 5 different spheres (physical symptoms, physical well-being, psychological symptoms, existential well-being and support) showed a statistically significant difference in quality of life between dialysis and transplant patients wherein the quality of life of kidney transplant patients is 18.12% greater. Another study showed that KT provides greater survival benefits to patients with end-stage renal disease, at less cost.

Table 1: Studies on deceased donor kidney transplant in the Philippines.

Author	*n*	KT Period	Immunosuppression	Induction Therapy	Patient Survival (%)	Graft Survival (%)
Liquete [6]	50	1983–1988	CyA+pred CyA+aza+pred	None	1 year–96 3 year–81	1 year–72 5year–50
Magcalas [7]	228	1984–1996	CyA+pred CyA+aza+pred	none	1 year–81 5 year–60 10 year -48	1 year–0 5 year–42 10 year–22
Ninalga [8]	71	1995–2001	CyA+aza+pred (46.5%) CyA+MMF+pred (46.5%) Tacro+aza+pred (2.8%) Tacro+MMF+pred (4.2%)	None (84.5%) IL-2 blocker (15.5%)	1 year–80 3 year–69	1 year–65 3 year–48
Overio [9]	156	2007– 2010	Tacrolimus based (96.8%) CyA based (3.2%)	IL- 2 blocker (62.2%) Polyclonal antibody (37.8%)	1 year–94 3 year–90	1 year–97 3 year–96

CyA: Cyclosporine; pred: prednisone; aza: azathioprine; tacro: tacrolimus; MMF: mycophenolate mofetil

Table 2: Demographic profile of recipients.

Characteristics		Frequency	Percentage
Age (years)	Less than 50 years old	71	78
	50 years old and above	20	22
Gender	Male	60	65.9
	Female	31	34.1
Presence of Diabetes Mellitus	Yes	14	15.4
	No	77	84.6
Primary Renal Disease	Chronic glomerulonephritis	58	63.7
	Diabetic nephropathy	17	18.7
	Hypertensive nephrosclerosis	6	6.6
	Chronic pyelonephritis	3	3.3
	Autosomal dominant polycystic kidney disease	5	5.5
	Others	2	2.2
Number of HLA-ABDR mismatch	0	1	1.1
	1	6	6.6
	2	21	23.1
	3	36	39.6
	4	18	19.8
	5	9	9.9
Number of DR matches	0	24	26.4
	1	56	61.5
	2	11	12.1
Panel Reactive Antibody (PRA)	Class 1>20%	2	3.6
	<20%	54	96.4
	Class 2>20%	0	0
	<20%	56	100
	No data	35	
Immunosuppressive Agents	Tacrolimus-based	59	64.8
	CyA-based	27	29.7
	Sirolimus- based	5	5.5
Induction Therapy	None	9	9.9
	Basiliximab	53	58.2
	Daclizumab	5	5.5
	Alemtuzumab	24	26.4

There is an increasing prevalence of ESRD and the demand for KT is increasing. Majority comprise living donation and unfortunately decease donation has not increase at an equivalent rate to meet the demand for KT [4]. In the Philippines, there are 10,000–12,000 new cases of ESRD annually [5]. In which 50% to 60% will need KT but only 10% is done. Of those being transplanted, 90% were from living donors and only 10% from deceased organ donation.

Various studies were done in the Philippines regarding outcome of deceased donor KT as shown in Table 1 [6-8]. These studies showed a remarkable improvement in the outcome of deceased donor KT.

Table 3: Causes of death.

Cause of Death	Frequency (*n*=13)	Percentage	Period of Death Post-KT (years)	
			<5	≥ 5
Infection Pneumonia (10)	10	76.9	9	1
Cardiovascular	2	15.4	1	1
Pulmonary embolism	1	7.7	1	0

Table 4: Recipient factors influencing 7-years patient survival.

Patient Survival					
Factors	**No. of Events**	**Censored**	**Estimated Mean Survival (in years)**	**Log-rank Statistic Value**	***P* Value**
Recipient Age					
Less than 50 y/o (*n*=71)	9	62	6.465	0.784	0.376
50 y/o and above (*n*=20)	4	16	5.8		
Recipient Gender					
Female (*n*=31)	4	27	6.29	0.058	0.809
Male (*n*=60)	9	51	6.333		
Primary Renal Disease					
Glomerulonephritis (*n*=58)	9	49	*No estimates are computed because most cases are censored.*	1.833	0.872
Diabetic Nephropathy (*n*=17)	3	14			
HPN (*n*=6)	1	5			
CPN (*n*=3)	0	3			
APKD (*n*=5)	0	5			
others (*n*=2)	0	2			
DM					
yes (*n*=14)	2	12	6.143	0.001	0.977
no (*n*=77)	11	66	6.351		
Induction					
none (*n*=9)	0	9	*No estimates are computed because most cases are censored.*	1.582	0.208
with induction (*n*=82)	13	69			
Immunosupression(ISA)					
CYA base (*n*=27)	6	21	*No estimates are computed because most cases are censored.*	2.468	0.291
Tacrolimus base (*n*=59)	7	52			
Sirolimus base (*n*=5)	0	5			
PRA*I*					
<20% (*n*=54)	7	47	*No estimates are computed because most cases are censored.*	0.283	0.595
>20% (*n*=2)	0	2			
PRA*II*					
<20% (*n*=56)	7	49	6.393	*No comparison analysis is performed because the factor variable has only one value for every stratum.*	
>20% (*n*=0)					
DR Match					
0 (*n*=24)	4	20	6.25	0.417	0.812
1 (*n*=56)	7	49	6.429		
2 (*n*=11)	2	9	5.909		
AB MM					
0 (*n*=1)	0	1	*No estimates are computed because most cases are censored.*	4.328	0.503
1 (*n*=6)	1	5			
2 (*n*=21)	4	17			
3 (*n*=36)	7	29			
4 (*n*=18)	0	18			
5 (*n*=9)	1	8			

Table 5: Recipient factors influencing 7-years graft survival.

Graft Survival					
Factors	**No. of Events**	**Censored**	**Estimated Mean Survival (in years)**	**Log-rank Statistic Value**	***P* Value**
Recipient Age					
Less than 50 y/o (*n*=71)	24	47	5.592	1.906	0.167
50 y/o and above (*n*=20)	3	17	6.231		
Recipient Gender					
Female (*n*=31)	8	23	5.903	0.374	0.541
Male (*n*=60)	19	41	5.621		
PRD- Renal Disease					
Glomerulonephritis(*n*=58)	17	41	5.817	1.222	0.943
Diabetic Nephropathy (*n*=17)	6	11	5.223		
HPN (*n*=6)	1	5	6		
CPN (*n*=3)	1	2	5.333		
APKD (*n*=5)	1	4	5.8		
others (*n*=2)	1	1	6.5		
DM					
yes (*n*=14)	5	9	5.13	0.541	0.462
no (*n*=77)	22	55	5.823		
Induction					
none (*n*=9)	1	8	6.444	1.558	0.212
with induction (*n*=82)	26	56	5.641		
Immunosupression (ISA)					
CYA base (*n*=27)	9	18	5.453	0.488	0.783
Tacrolimus base (*n*=59)	16	43	5.768		
Sirolimus base (*n*=5)	2	3	6.6		
PRA *I*					
<20% (*n*=54)	18	36	5.613	0.05	0.824
>20%(*n*=2)	1	1	7		
PRA *II*					
<20% (*n*=56)	19	37	5.663	*No comparison analysis is performed because the factor variable has only one value for every stratum.*	
>20% (*n*=0)					
DR Match					
0 (*n*=24)	6	18	6.009	0.553	0.758
1 (*n*=56)	17	39	5.665		
2 (*n*=11)	4	7	5.364		
AB MM					
0 (*n*=1)	0	1	*No estimates are computed because most cases are censored.*	5.806	0.326
1 (*n*=6)	0	6			
2 (*n*=21)	7	14			
3 (*n*=36)	14	22			
4 (*n*=18)	5	13			
5 (*n*=9)	1	8			

However, majority had 3 years as the longest follow up.

This study was conducted to determine the long-term outcome of deceased donor KT from 2002 to 2007.

Objectives

General objectives

- To determine the long term graft and recipient outcome of deceased donor renal transplantation at the National Kidney and Transplant Institute from 2002 to 2007
- To determine the donor and recipient factors that affect graft and recipient survival

Specific objectives

- To describe the recipients' demographic profile
- To determine the incidence of graft and patient survival rate among recipients of deceased donor KT at 7 years post-KT

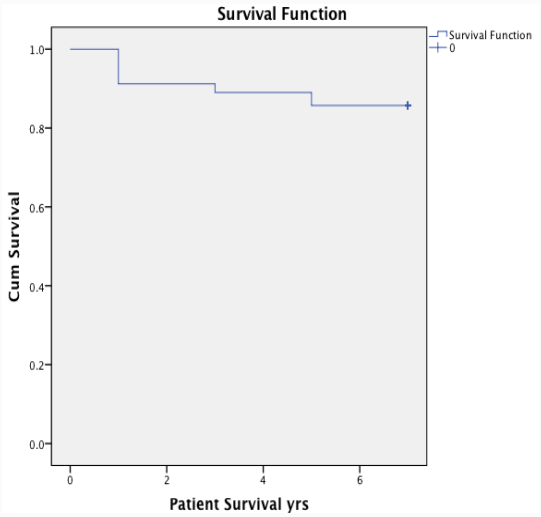

Figure 1: Kaplan Meier patient survival rate.

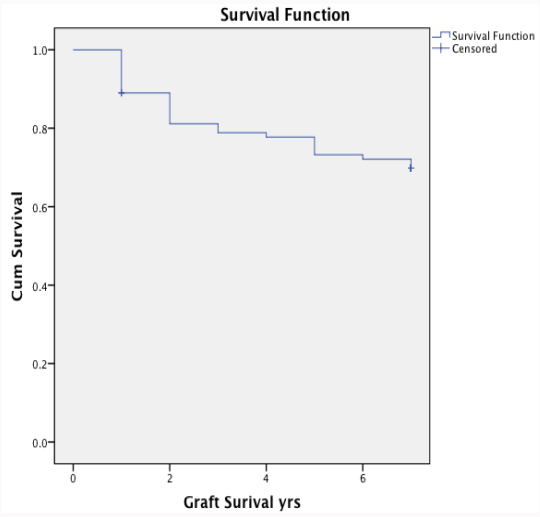

Figure 2: Kaplan Meier graft survival rate.

Table 6: Donor factors influencing 7-years patient survival.

Patient Survival					
Factors	**No. of Events**	**Censored**	**Estimated Mean Survival (in years)**	**Log-rank Statistic Value**	***P* Value**
Donor Age					
20 y/o and below (*n*=21)	1	20	6.714	4.605	0.1
21-40 y/o (*n*=61)	9	52	6.377		
41y/o and above (*n*=9)	3	6	5		
Donor Gender					
Female (*n*=13)	3	10	5.615	1.086	0.297
Male (*n*=78)	10	68	6.436		
Cold Ischemia Time					
<12 (*n*=24)	2	22	6.833	6.81	***0.033***
12- 24 (*n*=44)	4	40	6.455		
>24 (*n*=23)	7	16	5.522		

- To describe the recipients' cause of mortality
- To identify donor and recipient factors that significantly influences graft and patient survival at 7 years post KT

Methodology

Research Design: Retrospective cohort study.

Study Population: All patients are ≥ 18 years of age who underwent primary deceased donor KT from January 2002 to December 2007 at the National Kidney and Transplant Institute was included in this study. Excluded are pediatric patients, foreigners and those who are lost to follow up for at least 12 months post KT.

Materials and Methods

The following data were reviewed and collected from medical records and Philippine Renal Disease Registry (PRDR): a) recipients' demographic characteristics such as age, gender, cause of kidney disease, presence of diabetes mellitus, immunosuppressive regimen, induction therapy and immunologic status (Panel reactive antibody (PRA), number of HLA-ABDR mismatches and HLA-DR mismatches); b) donor factors such as age, gender and cold ischemia time (CIT).

Patients were followed up to 7 years post-KT to determine graft and patient survival.

Definition of terms

- Patient survival is the survival from the date of transplant until the date of death.
- Graft survival is the presence of renal function adequate to prevent the patient from resuming maintenance dialysis.
- Graft loss is patient's permanent return to dialysis.

Statistical analysis

The demographic profile of recipients and donors were expressed as frequency count, percentage and mean with standard deviation. Kaplan Meier was used to determine graft and patient's survival rate. To establish correlation between certain factors and survival, logistic regression analysis was utilized.

Ethical consideration

Confidentiality of the subjects was maintained. Anonymity was ensured and each patient was assigned a case number.

Results

From January 2002 to December 2007, a total of 1,598 KT were

Table 7: Donor factors influencing 7-years graft survival.

Graft Survival					
Factors	**No. of Events**	**Censored**	**Estimated Mean Survival (in years)**	**Log-rank Statistic Value**	***P* Value**
Donor Age					
20 y/o and below (*n*=21)	4	17	5.952	3.142	0.208
21-40 y/o (*n*=61)	19	42	5.841		
41y/o and above (*n*=9)	4	5	4.333		
Donor Gender					
Female (*n*=13)	8	5	3.692	11.055	***0.001***
Male (*n*=78)	19	59	6.06		
Cold Ischemia Time					
<12 (*n*=24)	6	18	6.417	0.674	0.714
12- 24 (*n*=44)	14	30	5.523		
>24 (*n*=23)	7	16	5.348		

performed at the National Kidney and Transplant Institute, 1,488 (93.1%) were from living donors and 110 (6.9%) were from deceased donors. Among the 110 recipients of deceased grafts, 91 (82.7%) patients were included in this study and 19 (17.3%) patients were excluded due to the following reasons: 3were foreigners; 10 pediatric patients and 6 had incomplete data.

Demographic characteristics

The mean recipient age was 40.40 ± 11.8 years and 65.9% were males. The primary renal diseases were chronic glomerulonephritis (63.7%), diabetic nephropathy (18.7%) and hypertensive nephrosclerosis (6.6%). There were 39.6% of patients who had 3 HLA mismatches and 61.5% with at least 1 DR match. Majority received induction therapy (90.1%) and 64.8% had tacrolimus-based immunosuppressive regimen (Table 2).

Graft and patient outcome

The survival rate at 1, 3, 5 and 7 years for patients was 91, 89, 86 and 86 percent while graft survival was 89, 79, 73 and 68 percent respectively (Figures 1 and 2). The leading cause of death was Infection (76%) followed by cardiovascular disease (14%). Most of the death occurred less than 5 years post-KT (Table 3).

N=91.

Factors associated with graft and patient survival at 7 years post-kidney transplant

Among the recipient factors studied, none were found to be significantly associated with graft and patient survival at 7 years post-KT (Tables 4 and 5).

Among the donor factors studied, cold ischemia time was significantly associated with patient survival rate among the listed and specified factors while the gender of the donor was significantly associated with graft survival rate.

Patient Survival Rate among patients was significantly different when grouped according to cold ischemia time. (Log Rank=6.81, *p*=0.033). Cold ischemia time with less than 12 had highest estimated mean survival rate (6.83 years), followed by 12-24 CIT (6.46 years). Patients with cold ischemia time greater than 24 had the lowest estimated survival rate (5.52 years) (Table 6). Graft survival of patients were significantly different when grouped according to donor's gender (Log Rank=11.055, *p* value=0.001). Patients who had male donors had significantly higher estimated survival rate (6.06 years) than patients with female donors (3.69 years) (Table 7).

Discussion

There has been continuous improvement in graft and patient survival from 1983 to 2010 [6-8].

Our study showed an improvement in graft survival when compared to studies done from 1983 to 2001 probably due to the improved immunosuppressive regimen, used of induction therapy and shorter cold ischemia time. When compared with the United States Renal Data System (USRDS) of 2013, our study was comparable in which their 1st, 3rd and 5th year patient survival rate were 94%, 86.6% and 75.5% while graft survival rates were 91.8%, 82.6% and 70.5% respectively [9].

The most common cause of death in our study was infection (76.9%) followed by cardiovascular disease (15.4%). Compared with the United States Renal Data System (USRDS) data the most common cause of death was cardiovascular disease (31%), infectious (19%) and malignancies (10%) [9]. However in a study in India of 160 deceased donor KT during 2006-2009, the most common cause of death was infection which was comparable to our study [10]. Factors for the high incidence of infections were unhygienic conditions, late presentation and diagnosis, high cost of life-saving antimicrobial agents and lack of sensitive and specific diagnostic tools that were either not available or were too expensive [10,11].

Among the recipient and donor factors studied, the donor's gender was noted to affect the 7-year graft survival in which male donor had better outcome than female (*p* value=0.001). This was similar to the study involving 464 renal transplant centers in Europe in which both patient and graft survival were worse with a female donor. Graft survival in female recipients of male donors was 48.4 ± 0.4 year vs. 46.9 ± 0.6 year for female donors (*p value*=0.0020). In male recipients, actuarial survival was 46.5 ± 0.3 year for male donor's vs. 42.1 ± 0.5 year for female donors (*p value*<0.0001). The assumption about the relative benefit of a male donor is that male kidneys have greater nephron number [12].

Another known risk factor that reduced long term survival of deceased KT was cold ischemia time. Patients with CIT of 12 h had a significant patient survival. This is explained because there was less rejection with shorter CIT hence no need to give solumedrol pulsing

hence no infection which is the main cause of patient mortality. The acute rejection with prolonged ischemia time could be reversed with solumedrol pulsing but could cause severe infection which may lead to death. United Network for Organ Sharing (UNOS) data noted a reduction in CIT during the 10-year period (1990–2000) with an overall reduction of 4.8 h and noted improvement in 3-year graft survival (80% in 1996–2000 vs. 72% in 1990–1995; $p<0.001$) [13]. Another study showed that CIT had a significant effect on the 6-year graft survival, a 10-hour increase in CIT was associated with a hazard risk ratio (HRR) of 1.20 for graft failure ($p<0.001$) [14]. In our study, CIT <12 h showed better 7-year graft survival compared to CIT 12 h to 24 h and >24 h however it did not achieved statistical significance. In contrast, CIT influence on patient survival achieved statistical significance (*P* value=0.033). CIT with less than 12 h had highest estimated mean survival rate (6.83 years), followed by 12 h to 24 h CIT (6.46 years) and >24 h CIT had the lowest estimated survival rate (5.52 years).

Conclusion

The survival rate at 1st, 3rd, 5th and 7th years for kidney transplant patients in the Philippines was 91%, 89%, 86% and 86% while graft survival was 89%, 79%, 73% and 68% respectively which is comparable to international data like UNOS. The most common cause of death was infection followed by cardiovascular disease. Among the recipient and donor factors, the donor's gender had effect on the 7-year graft survival in which male deceased donor KT had better graft survival compared to females and cold ischemia time was significantly associated with patient survival rate with CIT of less than 12 h having better survival compared to CIT 12 h to 24 h and >24 h.

References

1. Oniscu GC, Brown H, Forsythe JLR. Impact of cadaveric renal transplantation on survival in patients listed for transplantation. J Am Soc Nephrol. 2005;16(6):1859-65.
2. Perovic S, Jankovic S. Renal transplantation vs hemodialysis: cost-effectiveness analysis. Vojnosanit Pregl. 2009;66(8):639-44.
3. Kalo Z, Jaray J, Nagy J. Economic evaluation of kidney transplantation versus hemodialysis in patients with end-stage renal disease in hungary. Prog Transplant. 2001;11(3):188-93.
4. Neylan J, Sayegh MH, Coffman TM, Danovitch GM, Krensky AM, Strom TB, et al. The allocation of cadaver kidneys for Transplantation in the United States: consensus and controversy. ASN Transplant Advisory Group. American Society of Nephrology. J Am Soc Nephrol. 1999;10(10):2237-43.
5. Philippine Renal Registry 2010 Annual Report. Philippines: Department of Health; 2010.
6. Liquete R. Long Term Outcome of Cadaveric Kidney Patients. Philipp J Surg Spls. 1990;45(3):99-101.
7. Magcalas W, Liquete R. Long Term Outcome of Cadaver Kidney Recipients. Natl Kidney Transplant Inst Proc. 1996;1:1-8.
8. Ninalga HD, Danguilan RA, Tomacurz YT, Casasola CC, Liquete RM, Ona TE, et al. Graft and recipient outcome of cadaveric transplantation at the National Kidney and Transplant Institute from 1995-2001. Phillip J Nephrol. 2005;1:63-70.
9. Annual Data Report. Renal Transplantation Vol. 2. Michigan: Unites States Renal Data System (USRDS); 2013. p. 283-94.
10. Gumber MR, Kute VB, Goplani KR, Shah PR, Patel HV, Vanikar AV, et al. Deceased donor organ transplantation - A single-center experience. Indian J Nephrol. 2011;21(3):182-5.
11. Jha V, Chugh S, Chugh KS. Infections in dialysis and transplant patients in tropical countries. Kidney Int. 2000;57(74):S85-93.
12. Zeier M, Dohler B, Opelz G, Ritz E. The effect of donor gender on graft survival. J Am Soc Nephrol. 2002;13(10):2570-6.
13. Salahudeen AK, May W. Reduction in cold ischemia time of renal allografts in the u.s over the last decade. Transplant Proc. 2008;40(5):1285-9.
14. Salahudeen AK, Haider N, May W. Cold ischemia and the reduced long-term survival of cadaveric renal allografts. Kidney Int. 2004;65(2):713-8.