Proyecto Prometeo II

La función renal postrasplante como marcador de supervivencia: análisis de la evidencia

24 y 25 de octubre de 2014
Alcalá de Henares

Dossier bibliográfico

Grupo II | **Función renal inicial como marcador de supervivencia a largo plazo**

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GRUPO 2-Función renal inicial como marcador de supervivencia a largo plazo (ISABEL BENEYTO)

	Apellidos	Nombre	Hospital	Ciudad	Artículos asignados	Nº Art.
1	Alonso Melgar	Ángel	Hospital Universitario La Paz (TX Pediatricos)	Madrid	**1. Evolving experience using kidneys from deceased donors with terminal acute kidney injury.** J Am Coll Surg. 2013 Apr;216(4):645-55; discussion 655-6. doi: 10.1016/j.jamcollsurg.2012.12.020. Epub 2013 Feb 6. Farney AC1, Rogers J, Orlando G, al-Geizawi S, Buckley M, Farooq U, al-Shraideh Y, Stratta RJ. **2. Kidney transplantation from donation after cardiac death donors: lack of impact of delayed graft function on post-transplant outcomes.** Clin Transplant. 2011 Mar-Apr;25(2):255-64. doi: 10.1111/j.1399-0012.2010.01241.x. Singh RP, Farney AC, Rogers J, Zuckerman J, Reeves-Daniel A, Hartmann E, Iskandar S, Adams P, Stratta RJ	**11** **37**
2	**Beneyto Castelló**	**Isabel**	**Hospital Universitario La Fe**	**Valencia**	**1. Similar impact of slow and delayed graft function on renal allograft outcome and function.** Transplant Proc. 2005 Apr;37(3):1431-2. Rodrigo E, Fernández-Fresnedo G, Ruiz JC, Piñera C, Palomar R, González-Cotorruelo J, Zubimendi JA, De Francisco AL, Sanz de Castro S, Arias M. **2. Postrasplant renal functionin the fist year predicts long term kidney** Kidney Int 2002; 62 (1):311 Hariharan s el al	124 153
3	Cofan Pujol	Frederic	Hospital Clínic	Barcelona	**1. Long-term allograft survival after kidney transplantation.** Transplant Proc. 2013 Dec;45(10):3599-602. doi: 10.1016/j.transproceed.2013.09.015. Gómez EG, Hernández JP, López FJ, Garcia JR, Montemayor VG, Curado FA, Vallejo ML, López JC, Cabello MD, Aljama P, Tapia MJ. **2. Impact of early graft function on 10-year graft survival in recipients of kidneys from standard- or expanded-criteria donors.** Transplantation. 2013 Jul 27;96(2):176-81. doi: 10.1097/TP.0b013e318297443b. Smail N, Tchervenkov J, Paraskevas S, Baran D, Mucsi I, Hassanain M, Chaudhury P, Cantarovich M. **3. Risk factors for delayed kidney function and impact of delayed function on patient and graft survival in adult graft recipients.** Clin Transplant. 2005 Jun;19(3):391-8. Pieringer H, Biesenbach G.	**3** **5** **121**
4	Serra	Núria	Fundación Puigvert	Barcelona	**1. Renal perfusion pump vs cold storage for donation after cardiac death kidneys: a systematic review.** J Urol. 2013 Jun;189(6):2214-20. doi: 10.1016/j.juro.2012.11.173. Epub 2012 Dec 3. Bathini V, McGregor T, McAlister VC, Luke PP, Sener A. **2. Creatinine reduction ratio: a useful marker to identify medium and high-risk renal transplants.** Transplantation. 2010 Jan 15;89(1):97-103. doi: 10.1097/TP.0b013e3181be3dd1. Vilar E, Varagunam M, Yaqoob MM, Raftery M, Thuraisingham R.	**8** **39**
5	Errasti	Pedro	Clínica Universitaria de Navarra	Pamplona	**1. Intermediate early graft function is associated with increased incidence of graft loss and worse long-term graft function in kidney transplantation.** Transplant Proc. 2013 Apr;45(3):1070-2.doi:10.1016/j.transproceed.2013.02.013. Raimundo M, Guerra J, Teixeira C, Santana A, Silva S, Homens CM, da Costa AG. **2. Delayed graft function and the risk for death with a functioning graft.** J Am Soc Nephrol. 2010 Jan;21(1):153-61. doi: 10.1681/ASN.2009040412. Epub 2009 Oct 29. Tapiawala SN, Tinckam KJ, Cardella CJ, Schiff J, Cattran DC, Cole EH, Kim SJ.	**12** **43**
6	Fijo López-Viota	Julia	Hospital Virgen del Rocío (TX Pediátrico)	Sevilla	**1. Delayed renal graft function: risk factors and impact on the outcome of transplantation.** Transplant Proc. 2011 Jan-Feb;43(1):100-5. doi: 10.1016/j.transproceed.2010.12.023. Moreira P, Sá H, Figueiredo A, Mota A. **2. A retrospective analysis of long-term graft survival in 61 pediatric renal transplant recipients: A single-center experience** Ann Transplant, 2013; 18: 497-504 Ismail Sert, Önder Yavascan, Cem Tugmen, Orhan Deniz Kara, Selcuk Kılınc, Sait M. Dogan, Alkan Bal, Eyüp Kebabcı, Caner Alparslan, Cezmi Karaca, Nejat Aksu **3. NAPRTCS 2010** Annual Transplant Reprt	**32** **152** **155**

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8	Jimeno	Luisa	Hospital Virgen de la Arrixaca	Murcia	**1. Increased urinary CCL2: Cr ratio at 6 months is associated with late renal allograft loss.** Transplantation. 2013 Feb 27;95(4):595-602. doi: 10.1097/TP.0b013e31826690fd. Ho J, Wiebe C, Rush DN, Rigatto C, Storsley L, Karpinski M, Gao A, Gibson IW, Nickerson PW. **2. First year renal function as a predictor of kidney allograft outcome.** Transplant Proc. 2009 Apr;41(3):846-8. doi: 10.1016/j.transproceed.2009.01.066. Resende L, Guerra J, Santana A, Mil-Homens C, Abreu F, da Costa AG.	**15** **48**
9	López Oliva	María	Hospital Universitario La Paz	Madrid	**1. Impact of donor age on long-term outcomes after delayed graft function: 10-year follow-up.** Transpl Int. 2013 Feb;26(2):162-9. doi: 10.1111/tri.12016. Epub 2012 Dec 1. Lapointe I, Lachance JG, Noël R, Côté I, Caumartin Y, Agharazii M, Houde I, Rousseau-Gagnon M, Kim SJ, De Serres SA. **2. Delayed graft function has an equally bad impact on deceased donor renal graft survival in both standard criteria donors and expanded criteria donors.** Transplant Proc. 2009 Jan-Feb;41(1):133-4. doi: 10.1016/j.transproceed.2008.10.044. Hassanain M, Tchervenkov J, Cantarovich M, Metrakos P, Paraskevas S, Keith D, Baran D, Fernandez M, Mangel R, Chaudhury P. **3. Delayed graft function in renal transplantation** Curr Opin Crit Care. 2004 Dec;10(6):489-98. Peeters P, Terryn W, Vanholder R, Lameire N	**16** **49** **130**
10	Pérez Sáez	María José	Hospital del Mar	Barcelona	**1. Hypothermic machine perfusion reduces delayed graft function and improves one-year graft survival of kidneys from expanded criteria donors: a meta-analysis.** PLoS One. 2013 Dec 10;8(12):e81826. doi: 10.1371/journal.pone.0081826. eCollection 2013. Jiao B, Liu S, Liu H, Cheng D, Cheng Y, Liu Y. **2. Very early serum creatinine as a surrogate marker for graft survival beyond 10 years.** J Nephrol. 2009 Jan-Feb;22(1):90-8. Pascual J, Marcén R, Zamora J, Fernández AM, Burgos FJ, Villafruela JJ, Ortuño J.	**17** **51**
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12	Román Ortiz	Elena	Hospital Universitario La Fe	Valencia	**1. Delayed graft function, allograft and patient srvival in kidney transplantation.** Arab J Nephrol Transplant. 2012 Jan;5(1):19-24. Ghadiani MH, Peyrovi S, Mousavinasab SN, Jalalzadeh M. **2. Renal transplant dysfunction--importance quantified in comparison with traditional risk factors for cardiovascular disease and mortality.** Nephrol Dial Transplant. 2006 Aug;21(8):2282-9. Epub 2006 Mar 30. Soveri I, Holdaas H, Jardine A, Gimpelewicz C, Staffler B, Fellström	**23** **105**
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15	Sánchez Hernández	Rosa	Hospital General de Segovia	Segovia	**1. Slow Early Graft Function: A Neglected Entity after Renal Transplantation.** Nephron Clin Pract. 2012 Aug 24;120(4):c200-c204. [Epub ahead of print] Nel D, Vogel J, Muller E, Barday Z, Kahn D. **2. Reduced graft function (with or without dialysis) vs immediate graft function--a comparison of long-term renal allograft survival.** Nephrol Dial Transplant. 2006 Aug;21(8):2270-4. Epub 2006 May 23. Johnston O, O´kelly P, Spencer S, Donohoe J, Walshe JJ, Little DM, Hickey D, Conlon PJ.	**22** **104**

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Referencias Bibliográficas

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Con la colaboración de

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3. Transplant Proc. 2013 Dec;45(10):3599-602. doi: 10.1016/j.transproceed.2013.09.015.
Long-term allograft survival after kidney transplantation.

Gómez EG[1], Hernández JP, López FJ, Garcia JR, Montemayor VG, Curado FA, Vallejo ML, López JC, Cabello MD, Aljama P, Tapia MJ.

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Acceso al artículo

Abstract
BACKGROUND:
Technical and medical advances over the past few years have produced an important increase in the functionality of renal allografts. The aim of this study was to identify the factors associated with allograft survival 15 years after transplantation in our series.
METHODS:
A retrospective study of kidney transplantations was carried out at Reina Sofia Hospital in Cordoba from February 1979 to December 1997, with follow-up through June 2012. A subanalysis of the series was undertaken, and Kaplan-Meier analysis and Cox proportional hazards model regression used to achieve the main objective of the study.
RESULTS:
A total of 487 renal allografts with a mean follow-up of 114 months were studied, of which 37% (n = 180) survived for >15 years. Of the 180 patients, the main causes of graft failure were chronic allograft nephropathy in 29 (66%) and patient death in 13 (29.5%). Multivariate analysis identified the number of HLA mismatches (hazard ratio [HR] 1.25, 95% CI 1.01-1.56), panel reactive antibodies (HR 2.61, 95% CI 1.28-5.26), and delayed graft function (HR 11.25, 95% CI 1.33-95.28) as being significantly associated with graft loss after 15 years.
CONCLUSIONS:
The high immunologic risk of the patients was independently associated with graft loss. Delayed graft function was the most important factor in the speed of graft failure beyond 15 years.

5. Transplantation. 2013 Jul 27;96(2):176-81. doi: 10.1097/TP.0b013e318297443b.

Impact of early graft function on 10-year graft survival in recipients of kidneys from standard- or expanded-criteria donors.

Smail N[1], Tchervenkov J, Paraskevas S, Baran D, Mucsi I, Hassanain M, Chaudhury P, Cantarovich M.

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Acceso al artículo

Abstract

BACKGROUND:

The use of kidneys from expanded-criteria donors (ECD) is regarded with caution.

METHODS:

We compared 279 kidney transplant recipients (KTxR) from standard-criteria donors (SCD) and 237 from ECD, transplanted between January 1990 and December 2006. We evaluated the impact of immediate graft function (IGF), slow graft function (SGF), and delayed graft function (DGF) and the drop in estimated glomerular filtration rate (ΔeGFR) ≤ 30% or > 30% during the first year after transplantation on long-term patient and death-censored graft survival (DCGS).

RESULTS:

Ten-year patient survival was similar in SCD- or ECD-KTxR (P = 0.38). DCGS was better in SCD-KTxR versus ECD-KTxR (77.3% vs. 67.3%; P = 0.01). DCGS did not differ in either group experiencing IGF (P = 0.17) or DGF (P = 0.12). However, DCGS was worse in ECD-KTxR experiencing SGF (84.9% vs. 73.7%; P = 0.04). Predictors of DCGS were 1-year serum creatinine (hazard ratio, 1.03; P < 0.0001) and ΔeGFR > 30% between 1 and 12 months (Δ1-12eGFR) after transplantation (hazard ratio, 2.2; P = 0.02). In ECD-KTxR with IGF and more than 1-year follow-up, 10-year DCGS was better in those with Δ1-12eGFR ≤ 30% versus those with Δ1-12eGFR > 30% (83.8% vs. 53.6%; P = 0.01).

CONCLUSION:

Recipients of SCD or ECD kidneys with IGF or DGF had similar 10-year patient survival and DCGS. SGF had a worse impact on DCGS in ECD-KTxR. In addition to 1-year serum creatinine, Δ1-12eGFR > 30% is a negative predictor of DCGS. Larger studies should confirm if increasing the use of ECD, avoiding factors that contribute to SGF or DGF, and/or a decline in eGFR during the first year after transplantation may expand the donor pool and result in acceptable long-term outcomes.

8. J Urol. 2013 Jun;189(6):2214-20. doi: 10.1016/j.juro.2012.11.173. Epub 2012 Dec 3.

Renal perfusion pump vs cold storage for donation after cardiac death kidneys: a systematic review.

Bathini V[1], McGregor T, McAlister VC, Luke PP, Sener A.

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Acceso al artículo

Abstract

PURPOSE:

Static cold storage is generally used to preserve kidney allografts from deceased donors. Hypothermic machine perfusion may improve the outcome after transplantation but few studies with limited power have addressed this issue. We reviewed evidence of the effectiveness of storing kidneys from deceased donors after cardiac death before transplantation using cold static storage solution or pulsatile hypothermic machine perfusion.

MATERIALS AND METHODS:

We searched electronic databases in September 2011 for systematic reviews and/or meta-analyses, randomized, controlled trials and studies of other designs that compared delayed graft function and graft survival. Sources included The Cochrane Library, PubMed® and EMBASE®. Studies excluded from review included those that did not discriminate between donation after cardiac death and donation from a neurologically deceased donor. Primary outcomes were delayed graft function and 1-year graft survival. Statistical analysis was done using RevMan (http://ims.cochrane.org/revman).

RESULTS:

Nine studies qualified for review. Pulsatile perfusion pumped kidneys from donation after cardiac death donors had decreased delayed graft function compared to kidneys placed in cold storage (OR 0.64, 95% CI 0.43-0.95, p = 0.03). There was a trend toward improved 1-year graft survival in the pulsatile perfusion group but statistical significance was not attained (OR 0.74, 95% CI 0.48-1.13, p = 0.17).

CONCLUSIONS:

Pulsatile machine perfusion of donation after cardiac death kidneys appears to decrease the delayed graft function rate. We noted no benefit in 1-year graft survival. Due to the great heterogeneity among the trials as well as several confounding factors, the overall impact on allograft function and survival requires more study.

11. J Am Coll Surg. 2013 Apr;216(4):645-55; discussion 655-6. doi: 10.1016/j.jamcollsurg.2012.12.020. Epub 2013 Feb 6.

Evolving experience using kidneys from deceased donors with terminal acute kidney injury.

Farney AC[1], Rogers J, Orlando G, al-Geizawi S, Buckley M, Farooq U, al-Shraideh Y, Stratta RJ.

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Acceso al artículo

Abstract

BACKGROUND:

Kidney transplantation from deceased donors with terminal acute kidney injury (AKI) is not widely accepted.

STUDY DESIGN:

Acute kidney injury donor kidneys were defined by a doubling of the donor's admission serum creatinine (SCr) level and a terminal SCr level >2.0 mg/dL before organ recovery.

RESULTS:

Over 5.5 years, we transplanted 84 AKI donor kidneys, including 64 kidneys from standard criteria donors (SCD), 11 from expanded criteria donors (ECD), and 9 from donation after cardiac death (DCD) donors. Mean donor age was 36 years (range 15 to 68 years); mean admission and terminal donor SCr levels were 1.25 mg/dL and 3.2 mg/dL, respectively (mean terminal estimated glomerular filtration rate 25.5 mL/minute). With a mean follow-up of 35 months (range 6 to 70 months), actual patient and graft survival rates are 98% and 89%, respectively, which are numerically, but not statistically, higher than concurrent kidney transplants from brain-dead (non-AKI) SCDs at our center. Delayed graft function (DGF) occurred in 34 patients (40%). Mean 1-, 12-, and 24-month SCr levels were 1.8, 1.6, and 1.7 mg/dL, respectively. Delayed graft function was associated with lower 3-year graft survival for non-AKI SCD transplants (68% vs 90%, with and without DGF), but there was no impact of DGF on graft survival for AKI donor kidneys (89% vs 91%).

CONCLUSIONS:

Although AKI donor kidneys more commonly have DGF, the higher rate of DGF does not worsen graft outcomes. Kidneys from deceased donors with terminal AKI transplanted into appropriately selected patients have excellent medium-term outcomes and represent a method to safely expand the donor pool.

12. Transplant Proc. 2013 Apr;45(3):1070-2. doi: 10.1016/j.transproceed.2013.02.013.
Intermediate early graft function is associated with increased incidence of graft loss and worse long-term graft function in kidney transplantation.

Raimundo M[1], Guerra J, Teixeira C, Santana A, Silva S, Homens CM, da Costa AG.

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Acceso al artículo

Abstract

INTRODUCTION:

Intermediate early graft function is associated with increased incidence of graft loss and worse long-term graft function in kidney transplantation.

BACKGROUND:

Delayed graft function (DGF) is associated with premature graft loss, increased rate of allograft function decline, and greater incidence of acute rejection episodes (ARE). Regarding early intermediate graft function (IGF), these prognostic observations have not been clearly made. Our objective was to investigate the impact of IGF as compared with excellent graft function (EGF) on these outcomes.

METHODS:

Retrospective analysis included all patients who underwent transplantation in a tertiary care center between 1989 and 2009. Definitions are as follows: DGF, need for dialysis in the first 7 days posttransplantation; EGF, serum creatinine (sCr) <3 mg/dL at 5 days posttransplantation; IGF, absence of dialysis need but with a sCr >3 mg/dL at 5 days posttransplantation. For univariate analysis we performed Student t test, Mann- Whitney test, or Chi-square test, as appropriate. For survival analysis we performed Kaplan-Meier method to determine survival curves and we used the log-rank test for comparison. Multivariate logistic regression analysis was used to determine independent predictors of IGF and of graft survival.

RESULTS:

Five hundred seventy patients were included: 69.0% had EGF, 22.6% had IGF, and 8.4% had DGF. Patients with IGF had worse graft survival at 5 and 10 years posttransplantation (75% vs 92% and 69% vs 85%, respectively; P < .001 for both comparisons) and higher incidence of ARE (41% vs 27%; P = .001), compared with EGF. In multivariate analysis, IGF was independently associated with an increased risk of graft loss compared with EGF (odds ratio [OR], 2.40; 95% confidence interval [CI], 1.32-4.35; P = .004]. Donor age (OR, 1.03 per year; 95% CI, 1.02-1.05; P < .001) was the strongest predictor of the occurrence of IGF. IGF was also associated with worse long-term graft function until 7 years posttransplantation (mean glomerular filtration rate [GFR] 48.3 ± 18.9 vs 57.4 ± 20.4 mL/min/1.73 m(2); P = .008).

CONCLUSIONS:

IGF, as DGF, is associated with increased rates of graft loss and ARE, as well as worse long- term graft function. Donor age was the strongest risk factor for the occurrence of IGF. This is especially relevant regarding the increasing use of extended criteria donors.

14. Rev Invest Clin. 2013 Mar-Apr;65(2):109-15.

[Risk factors in the development of delayed graft function in deceased donor kidney transplant recipients and their impact on patient and graft survival].

[Article in Spanish]

Pérez-Gutiérrez A[1], Morales-Buenrostro LE, Vilatobá-Chapa M, Mendoza-De-la-garza A, Vega-Vega O, Gabilondo-Pliego B, Alberú J.

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Abstract

BACKGROUND:

Delayed graft function (DGF) is an early complication of kidney transplant (KT) and it is related to a higher incidence of acute rejection (AR) and lower graft survival. The incidence of DGF ranges from 2 to 29% in different series. Several risk factors for DGF have been described, including inotropic use in the deceased donor, long cold ischemia time, cardiovascular brain death, age > 55 years, hypovolemia, previous transplant, preformed antibodies and OKT3 use.

MATERIAL AND METHODS:

This study is a retrospective cohort of the kidney transplant recipients (KTR) of deceased donors from 1990 to 2009, at the INCMNSZ. We analyzed the incidence of DGF, risk factors associated to its development, and patient and graft outcome. To compare the groups, we used chi2 test or Student's t test for categorical and numeric variables, respectively. Patient and graft survival were calculated using Kaplan-Meier method; a p value < 0.05 was considered statistically significant.

RESULTS:

Data from 105 KTR were analyzed. DGF occurred in 21%, AR in 27%, graft loss in 15.2%. The only risk factor associated to DGF was brain death due to vascular disease (p = 0.028).

CONCLUSIONS:

Brain death due to vascular disease was the only risk factor associated to DGF. A non-significant higher incidence of AR was observed in patients with DGF. Survival was significantly lower in patients who developed DGF compared to those without DGF, and it was not related to renal function.

15. Transplantation. 2013 Feb 27;95(4):595-602. doi: 10.1097/TP.0b013e31826690fd.
Increased urinary CCL2: Cr ratio at 6 months is associated with late renal allograft loss.
Ho J[1], Wiebe C, Rush DN, Rigatto C, Storsley L, Karpinski M, Gao A, Gibson IW, Nickerson PW.

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Acceso al artículo

Abstract
BACKGROUND:
Early noninvasive markers that identify patients at risk of renal allograft loss may stratify patients for more intensive monitoring or therapy. CCL2 is a CCR2 receptor chemokine that is a chemoattractant protein for monocytes/macrophages, T cells, and natural killer cells. We have previously demonstrated in a multicenter cohort that urinary CCL2 at 6 months is an independent predictor for the development of IFTA at 24 months. The goal of this study was to determine if early urinary CCL2 is a predictor of graft loss in an independent patient cohort.
METHODS:
A prospective, observational cohort study was conducted in the Transplant Manitoba Adult Kidney Program (n=231 patients) from 1997 to 2008. Six-month urinary CCL2 was measured by ELISA, corrected for urinary creatinine, and correlated with long-term graft outcomes.
RESULTS:
Urine CCL2: Cr at 6 months was significantly associated with death-censored graft loss (HR, 2.42; 95% CI, 1.54-3.82, P<0.0001). On multivariate analysis, urinary CCL2: Cr at 6 months remained an independent predictor of death-censored graft loss (HR, 2.20; 95% CI, 1.18-4.10, P=0.01) after adjustment for pretransplant/de novo donor-specific antibody and delayed graft function. An early posttransplant (≤6 months) multivariate model of CCL2, recipient age, and delayed graft function yielded an AUC 0.87 for prediction of death-censored graft loss. A cutoff value of urinary CCL2: Cr 34.8 ng/mmol yielded a strong positive predictive value of 0.96.
CONCLUSIONS:
This study confirms in an independent prospective cohort that early urinary CCL2 at 6 months is a noninvasive, independent predictor for late renal allograft loss.

16. Transpl Int. 2013 Feb;26(2):162-9. doi: 10.1111/tri.12016. Epub 2012 Dec 1.

Impact of donor age on long-term outcomes after delayed graft function: 10-year follow-up.

Lapointe I[1], Lachance JG, Noël R, Côté I, Caumartin Y, Agharazii M, Houde I, Rousseau-Gagnon M, Kim SJ, De Serres SA.

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Acceso al artículo

Abstract

Delayed graft function (DGF) has a negative impact on graft survival in donation after brain death (DBD) but not for donation after cardiac death (DCD) kidneys. However, older donor age is associated with graft loss in DCD transplants. We sought to examine the interaction between donor age and DGF in DBD kidneys. This is a single-center, retrospective review of 657 consecutive DBD recipients transplanted between 1990 and 2005. We stratified the cohort by decades of donor age and studied the association between DGF and graft failure using Cox models. The risk of graft loss associated with DGF was not significantly increased for donor age below 60 years (adjusted hazard ratio [aHR] 1.12, 1.51, and 0.90, respectively, for age <40, 41-50 and 51-60 years) but significantly increased after 60 years (aHR 2.67; P = 0.019). Analysis of death-censored graft failure yielded similar results for donor age below 60 years and showed a substantially increased risk with donors above 60 years (aHR 6.98, P = 0.002). This analysis reveals an unexpectedly high impact of older donor age on the association between DGF and renal transplant outcomes. Further research is needed to determine the best use of kidneys from donors above 60 years old, where DGF is expected.

17. PLoS One. 2013 Dec 10;8(12):e81826. doi: 10.1371/journal.pone.0081826. eCollection 2013.
Hypothermic machine perfusion reduces delayed graft function and improves one-year graft survival of kidneys from expanded criteria donors: a meta-analysis.

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Acceso al artículo

Abstract
BACKGROUND:
Expanded criteria donors (ECDs) are currently accepted as potential sources to increase the donor pool and to provide more chances of kidney transplantation for elderly recipients who would not survive long waiting periods. Hypothermic machine perfusion (HMP) is designed to mitigate the deleterious effects of simple cold storage (CS) on the quality of preserved organs, particularly when the donor is in a marginal status.
METHODS:
We compared the transplant outcomes in patients receiving ECD kidneys with either HMP or CS graft preservation. Articles from the MEDLINE, EMBASE and Cochrane Library databases were searched and all studies reporting outcomes from HMP versus CS methods of kidney preservation were included in this meta-analysis. The parameters analyzed included the incidence of delayed graft function (DGF), primary non-function (PNF) and one-year graft and patient survival.
RESULTS:
A total of seven studies qualified for the review, involving 2374 and 8716 kidney grafts with HMP or CS preservation respectively, all from ECD donors. The incidence of delayed graft function (DGF) was significantly reduced with an odd ratio(OR) of 0.59 (95% CI 0.54-0.66, P<0.001) and one-year graft survival was significantly improved with an OR of 1.12 (95% CI 1.03-1.21, P = 0.005) in HMP preservation compared to CS. However, there was no difference in the incidence of PNF (OR 0.54, 95% CI 0.21-1.40, P = 0.20), and one-year patient survival (OR 0.98, 95% CI 0.94-1.02, P = 0.36) between HMP and CS preservation.
CONCLUSIONS:
HMP was associated with a reduced incidence of DGF and an with increased one-year graft survival, but it was not associated with the incidence of PNF and one-year patient survival.
PMCID: PMC3858268 **Free PMC Article**

20. Transplant Proc. 2012 Nov;44(9):2795-802. doi: 10.1016/j.transproceed.2012.09.087.

Delayed graft function does not harm the future of donation-after-cardiac death in kidney transplantation.

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Acceso al artículo

Abstract

INTRODUCTION:

Delayed graft function (DGF) occurs more frequently in kidney transplants from donation after cardiac death (DCD) than from donation after brain death (DBD). We investigated the effect of DGF on posttransplantation outcomes among grafts from controlled DCD kidneys.

PATIENTS AND METHODS:

This single-center retrospective study recruited 80 controlled DCD kidneys transplanted from January 2005 to December 2011. Mean patient follow-up was 28.5 months.

RESULTS:

There were no primary nonfunction grafts; the DGF rate was 35.5%. Overall graft survival rates between groups with versus without DGF were 92.4% and 95.2% at 1 year, 92.4% and 87.1% at 3 years, and 84.7% and 87.1% at 5 years, respectively (P = not significant (NS)). Patients with versus without DGF showed the same survival rates at the corresponding time 92.4% vs 97.2%, 92.4% vs 93.9%, and 84.7% vs 93.9% (P = NS). Estimated glomerular filtration rate was significantly lower in the DGF compared with the non-DGF group at hospital discharge (29 vs 42 mL/min; P = .00) and at 6 months posttransplantation (46 vs 52 mL/min; P = .04), but the difference disappeared thereafter: 47 vs 52 mL/min at 1 year, 50 vs 48 mL/min at 3 years, and 54 vs 53 mL/min at 5 years (P = NS). DGF did not increase the risk of an acute rejection episode (29.6% vs 30.6%; P = NS) or rate of surgical complications (33.3% vs 26.5%; P = NS). However, DGF prolonged significantly the length of hospitalization in the DGF versus the non- DGF group (18.9 vs 13 days; P = .00). Donor body mass index (BMI) ≥ 30 kg/m(2), recipient BMI ≥30 kg/m(2), and pretransplantation dialysis duration increased the risk of DGF upon multivariate logistic regression analysis.

CONCLUSIONS:

Apart from the longer hospital stay, DGF had no deleterious impact on the future of kidney allografts from controlled DCD, which showed comparable graft and patient survivals, renal function, rejection rates, and surgical complications as a group without DGF. Therefore, DGF should no longer be considered to be a medical barrier to the use of kidney grafts from controlled DCD.

21. Clin Transplant. 2012 Sep-Oct;26(5):E536-43. doi: 10.1111/ctr.12029.

Delayed graft function requiring more than one-time dialysis treatment is associated with inferior clinical outcomes.

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Acceso al artículo

Abstract

Delayed graft function (DGF) is a common complication of deceased donor kidney transplantation with negative impact on clinical outcomes. In a single-center retrospective analysis, we compared patient and kidney survival, early renal function, and the incidence of acute rejection during the first year among all adult deceased donor kidney transplant patients without DGF, with DGF requiring one-time and/or more than one-time dialysis treatment between January 1, 2000, and December 31, 2008. Of 831 adult kidney transplant patients, 74 (8.9%) required one-time and 134 (16.1%) more than one-time dialysis treatment post-transplantation, respectively. While DGF patients with one-time dialysis treatment had comparable clinical outcomes to that of patients without DGF, patients with DGF requiring more than one-time dialysis treatment had a 45% increased risk for death (HR 1.45, 95% CI 1.02, 2.05, $p = 0.04$) after adjustment for the differences in demographic and baseline characteristics. Furthermore, DGF patients with more than one-time dialysis requirement displayed significantly lower renal function after recovery (OR 0.32, 95% CI 0.21, 0.49, $p < 0.001$, for eGFR ≥ 60 mL/min) and higher incidence of acute rejection during the first year (OR 1.66, 95% CI 1.11, 2.49, $p = 0.015$). Additional studies of therapeutic approaches to manage patients with prolonged DGF are needed.

22. Nephron Clin Pract. 2012 Aug 24;120(4):c200-c204. [Epub ahead of print]
Slow Early Graft Function: A Neglected Entity after Renal Transplantation.
Nel D[1], Vogel J, Muller E, Barday Z, Kahn D.

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Acceso al artículo

Abstract
Background: After renal transplantation, early graft function (EGF) can be divided into delayed graft function (DGF), slow graft function (SGF) and immediate graft function (IGF). DGF is well documented. However, when evaluating the long-term significance of early function, the literature shows conflicting definitions and inconsistent results. In addition, SGF, a new entity separate to DGF and IGF, is a recent and poorly understood development. Aim: To investigate the risk factors for and the impact of poor EGF (PEGF) on long-term outcome. Methods: This retrospective study reviewed the records of local adult patients who underwent renal transplantation at the Groote Schuur Hospital (Cape Town, South Africa) between 2004 and 2008. EGF was divided according to day 5 serum creatinine into IGF (serum creatinine <150 μmol/l), SGF (serum creatinine >150 but <450 μmol/l) and DGF (serum creatinine >450 μmol/l or dialysis in the first week). DGF and SGF together comprised PEGF, with IGF alone representing good EGF (GEGF). Results: A total of 121 patients (77 men, 44 women; mean age 39 years, range 14-67) were included in the study. Eighteen were excluded due to nephrectomy (n = 8), death (n = 6) or loss to follow-up (n = 4) within the first year. Analysis of cadaveric donors showed no significant risk factors for PEGF with the exception of cold ischaemic time, which differed significantly between the GEGF and PEGF groups, with means of 12 and 16 h, respectively (p = 0.013). Considering both living and cadaveric grafts, the 1-year estimated glomerular filtration rate (eGFR) was significantly different between IGF and DGF (p = 0.038) as well as between IGF and SGF (p = 0.028), with no significant difference between SGF and DGF (p > 0.05). A comparison of the PEGF and GEGF groups yielded significantly different 1-year eGFR values (60 and 50 ml/min, respectively; p = 0.07), with PEGF also associated with a longer hospital stay (20 vs. 14 days; p = 0.00005). Acute rejection was independently associated with a lower 1-year eGFR (p = 0.028), but in the absence of rejection, GEGF and PEGF remained significantly different with regards to 1-year eGFR (p = 0.024). Conclusions: SGF is not related to IGF but rather to DGF and should thus be regarded as a form of PEGF as opposed to GEGF. PEGF has a worse long-term outcome, and this indicates the need for increased efforts in its prevention and greater attention to its management.

23. Arab J Nephrol Transplant. 2012 Jan;5(1):19-24.

Delayed graft function, allograft and patient srvival in kidney transplantation.

Ghadiani MH[1], Peyrovi S, Mousavinasab SN, Jalalzadeh M.

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Acceso al artículo

Abstract

INTRODUCTION:

Delayed Graft Function (DGF) is a common complication of renal transplants and the long-term relation between DGF and survival of patients and grafts is not well established.

METHODS:

This is a historical cohort study of transplanted patients in Taleghani Hospital of Shahid Beheshti University in Iran between 1994 and 2010. Patients who required dialysis during the first week after transplantation were considered to have DGF. The patients' conditions were updated to determine existing graft function, graft loss or patients' death at one year and five years post transplantation in relation to the presence or absence of DGF.

RESULTS:

DGF complicated 67/385 transplants (17.4%). Causes included acute tubular necrosis (58.2%), accelerated rejection (29.9%), transplant renal artery thrombosis (9%) and renal vein thrombosis (3%). More kidneys in the DGF group were procured from cadaveric donors (6% versus 0.9%, P = 0.02). At hospital discharge, patients with DGF had significantly higher mean creatinine level (4.4 ± 2.8 versus 2.0 ± 1.7; P = 0.001) compared to other patients. They also had more early acute rejection episodes and more late acute rejection episodes (34.3% versus 2% and 16.4% versus 3%, respectively; P = 0.0001) compared to other patients. The proportion of functioning grafts was significantly lower in the DGF group at 1-year (53.7% versus 95.3%, P = 0.0001) and 5-years (22.4% versus 61.6%, P = 0.001) compared to patients without DGF.

CONCLUSION:

The DGF group had a significantly higher acute rejection rate and an increased risk of graft loss at one and five years.

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31. Transplant Proc. 2011 Jan-Feb;43(1):106-12. doi: 10.1016/j.transproceed.2010.12.034.
First-year renal function predicts long-term renal allograft loss.

Fonseca I[1], Almeida M, Martins LS, Santos J, Dias L, Lobato L, Henriques AC, Mendonça D.

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Acceso al artículo

Abstract
PURPOSE:
We performed a retrospective study to examine the impact on long-term graft survival of first-year posttransplantation renal function, as evaluated by serum creatinine.
PATIENTS AND METHODS:
We analyzed data from 1,273 adult kidney transplants performed between 1983 and 2008. All recipients >18 years old were included if their grafts had survived beyond 1 year, excluding patients simultaneously transplanted with other organs. Cox proportional hazards multivariable analysis was used to examine the relationship between first-year posttransplantation renal function and death-censored graft loss, adjusted for other variables. Renal function in the first year was expressed as serum creatinine levels at 1, 6, and 12 months as well as the change in creatinine between those 3 periods.
RESULTS:
Posttransplantation 1-month serum creatinine levels and change between 1 and 6 months were independent predictors of long-term graft loss. Multivariable analysis also identified donor age (increasing), acute rejection episode occurrence, recipient age at transplantation (decreasing), and gender (female) as independently predictive of graft failure, adjusting for other factors usually associated with graft loss, namely, pretransplantation time on dialysis, HLA mismatches, and delayed graft function. The predictive effect of creatininemia was sustained at 6 and 12 months, after adjusting for these covariates.
CONCLUSIONS:
Posttransplantation serum creatinine levels at 1, 6, and 12 months were independent predictors of graft survival, suggesting that they could be considered as surrogate endpoints for long-term death-censored graft loss.

32. Transplant Proc. 2011 Jan-Feb;43(1):100-5. doi: 10.1016/j.transproceed.2010.12.023.
Delayed renal graft function: risk factors and impact on the outcome of transplantation.
Moreira P[1], Sá H, Figueiredo A, Mota A.

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Acceso al artículo

Abstract
OBJECTIVES:
The objectives of this study were to determine whether delayed graft function (DGF) implied a higher incidence of poor prognostic markers and to determine its impact on renal transplantation outcomes, particularly graft and patient survivals.
METHODS:
This retrospective study included 997 cadaveric kidney transplantations between January 1, 1996 and December 31, 2007. Two groups were created: immediate diuresis (ID; n = 803; 80.5%) and DGF (n = 194; 19.5%).
RESULTS:
These donor related variables showed significant differences (P < .05): age (ID, 35.20 ± 15.681; DGF, 42.49 ± 16.316), weight (ID, 70.54 ± 12.896; DGF, 74.86 ± 14.402), death cause (stroke: ID, 24.9%; DGF, 42.6%), hourly urinary output (ID, 225.55 ± 168.107; DGF, 187.29 ± 125.623), and creatinine (ID, 1.004 ± 0.3737; DGF, 1.075 ± 0. 4148). The significant recipient-related age (ID, 42.95 ± 13.095; DGF, 45.57 ± 13.138), dialysis time ID, 39.41 ± 38.172; DGF, factors were as follows 56.14 ± 44.243), dialysis type, and comorbidities. The significant transplant-related variables were follows: cold ischemia time (ID, 19.489 ± 4.841; DGF, 21.469 ± 5.297) and surgery duration (ID, 2.549 ± 1.105; DGF, 3.028 ± 1.738). Acute rejection and chronic allograft nephropathy (CAN) were greater among the DGF group (ID, 27.3% and 15.0% and DGF, 55.2% and 34.0%, respectively). Average graft (ID, 127.8 months; DGF, 93.9 months) and patient survival (ID, 143.2 months; DGF, 125.6 months) were higher in patients with ID. Multivariate analysis identified these independent risk factors for graft loss: CAN (hazard ratio [HR], 3.30) and DGF (HR, 2.30) but neither had an influence on patient survival.
CONCLUSIONS:
DGF was associated with multiple risk factors and contributed to worse graft outcomes. It is an independent risk factor for graft loss and an important marker of other factors that affect decisively the outcome of renal transplantation.

37. Clin Transplant. 2011 Mar-Apr;25(2):255-64. doi: 10.1111/j.1399-0012.2010.01241.x.

Kidney transplantation from donation after cardiac death donors: lack of impact of delayed graft function on post-transplant outcomes.

Singh RP[1], Farney AC, Rogers J, Zuckerman J, Reeves-Daniel A, Hartmann E, Iskandar S, Adams P, Stratta RJ.

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Acceso al artículo

Abstract

INTRODUCTION:

Delayed graft function (DGF) is more common in recipients of kidney transplants from donation after cardiac death (DCD) donors compared to donation after brain death (DBD) donors.

METHODS:

Single-center retrospective study to evaluate the impact of DGF on controlled (Maastricht category III) DCD donor kidney transplant outcomes.

RESULTS:

From 10/01 to 6/08, 578 adult deceased donor kidney transplants were performed including 70 (12%) from DCD and 508 (88%) from DBD donors. Mean follow-up was 36 months. DCD donor kidney transplants had significantly greater rates of DGF (57% DCD vs. 21% DBD, $p < 0.0001$)) and acute rejection (29% DCD vs. 16% DBD, $p = 0.018$) compared to DBD donor kidney transplants, but patient and graft survival rates were similar. DBD donor kidney transplants with DGF (n = 109) had significantly greater rates of death-censored graft loss (12.5% DCD vs. 31% DBD), primary non-function (0 DCD vs. 10% DBD) and higher 2 year mean serum creatinine levels (1.4 DCD vs. 2.7 mg/dL DBD) compared to DCD donor kidney transplants with DGF (n = 40, all $p < 0.04$). On univariate analysis, the presence of acute rejection and older donor age were the only significant risk factors for death-censored graft loss in DCD donor kidney transplants, whereas DGF was not a risk factor.

CONCLUSION:

Despite higher rates of DGF and acute rejection in DCD donor kidney transplants, subsequent outcomes in DCD donor kidney transplants with DGF are better than in DBD donor kidney transplants experiencing DGF, and similar to outcomes in DCD donor kidney transplants without DGF.

39. Transplantation. 2010 Jan 15;89(1):97-103. doi: 10.1097/TP.0b013e3181be3dd1.

Creatinine reduction ratio: a useful marker to identify medium and high-risk renal transplants.

Vilar E[1], Varagunam M, Yaqoob MM, Raftery M, Thuraisingham R.

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Acceso al artículo

Abstract

INTRODUCTION:

Delayed graft function (DGF) has a major impact on long-term renal transplant survival. However, it is a diagnosis made retrospectively with little opportunity to modify treatment protocols. A classification based on creatinine reduction ratio between days 1 and 2 (CRR2) suggests that patients with CRR2 less than or equal to 30% (nondialysis requiring DGF [ND-DGF]) have similar outcomes to those with dialysis-requiring delayed graft function (D-DGF). We retrospectively applied this definition in our cohort of patients to examine outcomes.

METHODS:

We studied the association between CRR2 and graft outcomes in all 367 patients transplanted between 1996 and 2004 at our center. Patients were divided into the following three groups: IGF (immediate graft function; CRR2 >30%), D-DGF, and ND-DGF. Mean follow-up was 4.2 years.

RESULTS:

IGF accounted for 36% of patients, D-DGF for 22%, and ND-DGF for 42%. CRR2 was inversely correlated with serum creatinine on days 7, 30, 90, and 365 (r ranging from -0.65 to -0.22, P<0.001). Graft survival at 5 years was 98% (IGF), 74% (D-DGF), and 89% (ND-DGF). There was a significant difference in graft survival between IGF and D-DGF (P<0.001) and IGF and ND-DGF (P=0.005). In a multivariate analysis adjusting for recipient age and sex, donor age and sex, and human leukocyte antigen mismatch, graft failure was 2.4 times more likely to occur in patients with D-DGF than those with ND-DGF(P=0.02).

CONCLUSIONS:

Our study shows CRR2 influences long-term graft outcomes. Unlike the original description, patients with ND-DGF carry an intermediate risk and perhaps should be considered on day 2 for alternative treatment protocols.

43. J Am Soc Nephrol. 2010 Jan;21(1):153-61. doi: 10.1681/ASN.2009040412. Epub 2009 Oct 29.
Delayed graft function and the risk for death with a functioning graft.

Tapiawala SN[1], Tinckam KJ, Cardella CJ, Schiff J, Cattran DC, Cole EH, Kim SJ.

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Acceso al artículo

Abstract
Delayed graft function (DGF) associates with an increased risk for graft failure, but its link with death with graft function (DWGF) is unknown. We used the US Renal Data System to assemble a cohort of all first, adult, deceased-donor kidney transplant recipients from January 1, 1998, through December 31, 2004. In total, 11,542 (23%) of 50,246 recipients required at least one dialysis session in the first week after transplantation. Compared with patients without DGF, patients with DGF were significantly more likely to die with a functioning graft (relative hazard 1.83 [95% confidence interval 1.73 to 1.93] and 1.53 [95% CI 1.45 to 1.63] for unadjusted and fully adjusted models, respectively). The risk for DWGF was slightly higher among women with DGF than among men. There was no significant heterogeneity among other subgroups, and the results were robust to sensitivity analyses. Acute rejection within the first year attenuated the DGF-DWGF association. Cardiovascular and infectious deaths were slightly more prevalent in the DGF group, but the relative hazards of cause-specific death were similar between DWGF and deaths during total follow-up. In summary, DGF associates with an increased risk for DWGF; the mechanisms underlying the negative impact of DGF require further study.
PMCID: PMC2799285 **Free PMC Article**

45. Am J Transplant. 2009 Aug;9(8):1796-801. doi: 10.1111/j.1600-6143.2009.02692.x. Epub 2009 Jun 10.

Fate of the mate: the influence of delayed graft function in renal transplantation on the mate recipient.

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Acceso al artículo

Abstract
Delayed graft function (DGF) in a deceased-donor renal recipient is associated with allograft dysfunction 1-year posttransplant. There is limited research about the influence to allograft function on the mate of a DGF recipient over time. Using a retrospective cohort design, we studied 55 recipients from a single center. The primary outcome was the change in glomerular filtration rate (GFR) 1-year posttransplant. The secondary outcome was the GFR at baseline. We found that mates to DGF recipients had a mean change in GFR 1-year posttransplant of -11.2 mL/min, while the control group had a mean change of -0.4 mL/min. The difference in the primary outcome was significant ($p = 0.025$) in a multivariate analysis, adjusting for cold ischemic time, panel reactive antibody level, allograft loss, human leukocyte antibody (HLA)-B mismatches and HLA-DR mismatches. No significant difference between groups was found in baseline GFR. In conclusion, mates to DGF recipients had a significantly larger decline in allograft function 1-year posttransplant compared to controls with similar renal function at baseline. We believe strategies that may preserve allograft function in these'at-risk'recipients should be developed and tested.
Free Article

48. Transplant Proc. 2009 Apr;41(3):846-8. doi: 10.1016/j.transproceed.2009.01.066.
First year renal function as a predictor of kidney allograft outcome.

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Acceso al artículo

Abstract
BACKGROUND:
Several factors are known to have detrimental effects on kidney allograft function in the first year posttransplantation, which has been reported to be an important factor influencing long-term graft survival.
OBJECTIVES:
The objectives of this study were to evaluate risk factors for lower estimated glomerular filtration rate (eGFR) at 3 and 12 months posttransplantation and analyze the influence of first year allograft function on graft and patient survivals.
PATIENTS:
We performed a retrospective review of the clinical data from 433 cadaveric donor kidney transplantations in adults performed in our unit from May 1989 to May 2007.
RESULTS:
Donor female gender and nontraumatic cause of death, panel-reactive antibody (PRA) titer > or =50%, acute rejection episodes, and delayed graft function (DGF) were significant risk factors for a decreased eGFR at one year posttransplantation. Recipient and donor age showed negative correlations with eGFR at 3 and 12 months. A logistic regression model showed acute rejection episodes, DGF, donor age > or =55 years, donor female gender, and nontraumatic cause of donor death to be independent adverse risk factors for eGFR <60 mL/min at 3 and 12 months. Lower eGFRs at 3 and 12 months were associated with poorer allograft survival when data were censored for death with a functioning graft and patient survival. Multivariate analysis revealed that PRA titer > or =50%, acute rejection episodes, and eGFR <30mL/min at 12 months had adverse effects on allograft survival.
CONCLUSION:
Several factors influence kidney allograft function in the first year after transplantation. Kidney allograft function at 12 months predicted long-term graft survival.

49. Transplant Proc. 2009 Jan-Feb;41(1):133-4. doi: 10.1016/j.transproceed.2008.10.044.

Delayed graft function has an equally bad impact on deceased donor renal graft survival in both standard criteria donors and expanded criteria donors.

Hassanain M[1], Tchervenkov J, Cantarovich M, Metrakos P, Paraskevas S, Keith D, Baran D, Fernandez M, Mangel R, Chaudhury P.

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Acceso al artículo

Abstract

INTRODUCTION:

The use of expanded criteria donors (ECDs) is still limited because of inferior graft survival compared to standard criteria donors (SCDs). We assessed the impact of immediate graft function (IGF) on renal graft survival among recipients of SCD and ECD grafts to determine whether these kidneys performed equally well under "ideal" conditions favoring IGF.

METHODS:

We included all cadaveric renal transplants performed from 1990 to 2002 (n = 335). Delayed graft function (DGF) was defined as the need for dialysis in the first 7 days posttransplant. Slow graft function (SGF) and IGF were defined as a serum creatinine fall by <20% versus >20% in the first 24 hours posttransplant, respectively. Non-death censored actual graft survivals are reported herein.

RESULTS:

Seventy-two of the 335 subjects (21.5%) received organs from ECDs and displayed IGF in 54.7%, SGF 16.2%, and DGF 29.1%. Among SCDs, the SGF and DGF rates were 15.3% and 23.4%, respectively. In ECD, the SGF and DGF rates were 19.4% and 50% ($P < .02$). Actual graft survivals at 1 and 5 years was 86.3% and 70.4%, respectively. Patients with IGF had higher actual graft survival at 5 years compared to SGF and DGF (83.5% vs 74.1% vs 45.4%). DGF had an equally bad impact on actual 5-year graft survival in SCDs and ECDs (42.6% vs 50%).

CONCLUSION:

DGF has a strong detrimental impact on 5-year graft survival. There is a higher rate of DGF in ECD versus SCD kidneys. The detrimental impact on 5-year actual graft survival is equal in SCD and ECD kidneys. Minimizing DGF should be our goal.

51. J Nephrol. 2009 Jan-Feb;22(1):90-8.

Very early serum creatinine as a surrogate marker for graft survival beyond 10 years.

Pascual J[1], Marcén R, Zamora J, Fernández AM, Burgos FJ, Villafruela JJ, Ortuño J.

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Acceso al artículo

Abstract

BACKGROUND:

Available studies of early serum creatinine (SCr) as a surrogate marker for long-term graft loss are multicenter, registry-based or limited to 5- to 7-year survival.

METHODS:

This was a single-center observational retrospective study. SCr during the first year post-kidney transplant as an independent variable in determining long-term (>10-year) graft survival in 754 first cadaver kidney transplants was assessed with univariate and multivariate models.

RESULTS:

Kaplan-Meier survival estimates showed that recipient female sex, a transplant procedure performed after 1997, donor age under 55 years, immunosuppression including tacrolimus and/or mycophenolate mofetil and absence of acute rejection, were significantly related to better long-term graft survival. SCr at 1, 3, 6 and 12 months stratified into <or=1.5, 1.6-2 and >2 mg/dL groups was also strongly related to long-term graft survival. Multivariate Cox models showed that increased SCr at any point during the first year had a higher relative risk for ultimate graft loss.

CONCLUSIONS:

Early graft function is strongly correlated with long-term graft survival (>or=10 years). Mild differences in SCr (1.5 vs. 1.6-2 mg/dL) are associated with highly significant impact on long-term survival, longer than previously described. However, the "hard" predictive value of SCr as an isolated tool is not strong enough. Other early surrogate end points for graft loss are needed.

53. Nephrol Dial Transplant. 2009 Mar;24(3):1039-47. doi: 10.1093/ndt/gfn667. Epub 2008 Dec 22.

Association between delayed graft function and allograft and patient survival: a systematic review and meta-analysis.

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Acceso al artículo

Abstract

BACKGROUND:

Delayed graft function (DGF) is a common complication of renal transplantation. The short-term consequences of DGF are well known, but the long-term relationship between DGF and patient and graft survival is controversial in the published literature. We conducted a systematic review and meta-analysis to precisely estimate these relationships.

METHODS:

We performed a literature search for original studies published through March 2007 pertaining to long-term (>6 months) outcomes of DGF. The primary outcome was graft survival. Secondary outcomes were patient survival, acute rejection and kidney function.

RESULTS:

When compared to patients without DGF, patients with DGF had a 41% increased risk of graft loss (RR 1.41, 95% CI 1.27-1.56) at 3.2 years of follow-up. There was no significant relationship between DGF and patient survival at 5 years (RR 1.14, 95% CI 0.94-1.39). The mean creatinine in the non-DGF group was 1.6 mg/dl. Patients with DGF had a higher mean serum creatinine (0.66 mg/dl, 95% CI 0.57-0.74) compared to patients without DGF at 3.5 years of follow-up. DGF was associated with a 38% relative increase in the risk of acute rejection (RR 1.38, 95% CI 1.29-1.47).

CONCLUSION:

The results of this meta-analysis emphasize and quantify the long-term detrimental association between DGF and important graft outcomes like graft survival, acute rejection and renal function. Efforts to prevent and treat DGF should be aggressively investigated in order to improve graft survival given the deficit in the number of kidney donors.

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98. Transplant Proc. 2006 Dec;38(10):3377-81.

Immediate graft function positively affects long-term outcome of renal allografts from older but not from younger donors.

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Acceso al artículo

Abstract

There is disagreement about the impact of delayed graft function (DGF) on renal allograft outcome. This may depend on several variables including the age of the donor. We evaluated whether DGF could have different effects in recipients of kidneys from donors aged more than 60 years versus well-matched recipients of younger kidney donors. Patients were retrospectively subdivided into 3 groups. Immediate graft function (IGF), DGF without dialysis (DGF-ND), DGF requiring dialysis (DGF-D). DGF-ND and DGF-D occurred more frequently among 198 older than 198 younger donors (P = .016 and P = .044, respectively). The 5-year patient (96% vs 93%) and pure graft (96% vs 89%) survivals were significantly better in younger recipients, while the incidence of acute rejection was similar. After a mean follow-up of 66 +/- 44 months in older donor recipients, the graft survival was significantly better among IGF than patients in the DGF-ND (P = .046) or DGF-D (P = .003) groups. Instead, in younger recipients there was no difference in graft survival between IGD and DGF-ND. Only patients with DGF-D showed a significantly worse outcome. Upon multivariate analysis of older donors, their recipients, showed the pattern of graft function recovery to be the only variable associated with allograft outcome. Instead in younger donor recipients, acute rejection and time on dialysis were the main variables associated with a poor outcome. In older donor recipients, DGF was an independent variable associated with a poor graft outcome. In younger donor recipients, duration of dialysis and rejection were the most important predictors of poor graft outcomes.

104. Nephrol Dial Transplant. 2006 Aug;21(8):2270-4. Epub 2006 May 23.

Reduced graft function (with or without dialysis) vs immediate graft function--a comparison of long-term renal allograft survival.

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Acceso al artículo

Abstract

BACKGROUND:

Delayed graft function (DGF) is a common complication in cadaveric kidney transplants affecting graft outcome. However, the incidence of DGF differs widely between centres as its definition is very variable. The purpose of this study was to define a parameter for DGF and immediate graft function (IGF) and to compare the graft outcome between these groups at our centre.

METHODS:

The renal allograft function of 972 first cadaveric transplants performed between 1990 and 2001 in the Republic of Ireland was examined. The DGF and IGF were defined by a creatinine reduction ratio (CRR) between time 0 of transplantation and day 7 post-transplantation of <70 and >70%, respectively. Recipients with reduced graft function (DGF) not requiring dialysis were defined as slow graft function (SGF) patients. The serum creatinine at 3 months, 6 months, 1, 2 and 5 years after transplantation was compared between these groups of recipients. The graft survival rates at 1, 3 and 5 years and the graft half-life for DGF, SGF and IGF recipients were also assessed.

RESULTS:

Of the 972 renal transplant recipients, DGF was seen in 102 (10.5%) patients, SGF in 202 (20.8%) recipients and IGF in 668 (68.7%) patients. Serum creatinine levels were significantly different between the three groups at 3 and 6 months, 1, 2 and 5 years. Graft survival at 5 years for the DGF patients was 48.5%, 60.5% for SGF recipients and 75% for IGF patients with graft half-life of 4.9, 8.7 and 10.5 years, respectively.

CONCLUSION:

This study has shown that the CRR at day 7 correlates with renal function up to 5 years post-transplantation and with long-term graft survival. We have also demonstrated that amongst patients with reduced graft function after transplantation, two groups with significantly different outcomes exist.

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105. Nephrol Dial Transplant. 2006 Aug;21(8):2282-9. Epub 2006 Mar 30.

Renal transplant dysfunction--importance quantified in comparison with traditional risk factors for cardiovascular disease and mortality.

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Acceso al artículo

Abstract

BACKGROUND:

Renal transplant recipients (RTR) mainly die of premature cardiovascular disease. Traditional cardiovascular disease risk factors are prevalent in RTR. Additionally, non-traditional risk factors seem to contribute to the high risk. The impact of renal dysfunction was compared with traditional risk factors for cardiovascular morbidity and mortality in 1052 placebo-treated patients of the ALERT trial.

METHODS:

All patients were on cyclosporine-based immunosuppressive therapy, follow-up was 5-6 years and captured endpoints included cardiac death, non-cardiovascular death, all-cause mortality, major adverse cardiac event (MACE), non-fatal myocardial infarction (MI) and stroke.

RESULTS:

A calculated 84 micromol/l increase in serum creatinine was needed to double the risk for cardiac death, an increase of 104 micromol/l to double the risk for non-cardiovascular death and an increase of 92 micromol/l to double the risk for all-cause mortality. MACE risk was doubled if serum creatinine was elevated by 141 micromol/l, age was increased by 23 years, or LDL-cholesterol by 2 mmol/l. Diabetes increased the incidences of cardiac death, all-cause mortality, MACE, stroke and non-fatal MI. A serum creatinine increase of approximately 130 micromol/l, or approximately 20 years increase in age was calculated as similar in risk for cardiac death, all-cause mortality and MACE, and comparable to risk of diabetes in RTR.

CONCLUSION:

An increase in serum creatinine of 80-100 micromol/l doubles the risk for cardiac death, non-cardiovascular death and all-cause mortality in RTR. An increase of 130 micromol/l in serum creatinine or approximately 20 years increase in age is comparable to risk of diabetes.

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114. Transplantation. 2006 Jan 27;81(2):202-6.

Estimated one-year glomerular filtration rate is the best predictor of long-term graft function following renal transplant.

Salvadori M[1], Rosati A, Bock A, Chapman J, Dussol B, Fritsche L, Kliem V, Lebranchu Y, Oppenheimer F, Pohanka E, Tufveson G, Bertoni E.

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Acceso al artículo

Abstract

BACKGROUND:

Long-term success of renal transplantation depends upon the quality of the donor organ, avoidance of peritransplant and early posttransplant damage (rejection), and optimal maintenance of graft function after the first 6-12 months. Glomerular filtration rate (GFR) at 1 year is a standard way to evaluate short-term success, whereas calculated GFR at 5 years gives a better appreciation of long-term outcomes. The objective of this study was to assess the effect of various demographic and transplant-related parameters on renal function via GFR at 1 year and 5 years post transplantation, using univariate and multivariate data analysis.

METHODS:

Data on 1-year GFR were available from 10,397 patients, whereas 2,889 patients provided data on both 1-year and 5-year GFR. All patients were enrolled in the Neoral Multinational Observational Study in Transplantation (Neoral-MOST), an ongoing, prospective, observational study of adult renal transplant recipients.

RESULTS:

One-year GFR was the most relevant predictor for 5-year GFR. In a multifactorial analysis (ANCOVA) using 1-year GFR as a continuous variable, the effects of several highly relevant parameters from univariate analysis (such as acute rejection and delayed graft function) on 5-year GFR appeared to be fully mediated by their influence on 1-year GFR, whereas immunological risk factors like HLA match or previous transplantation had an ongoing effect on graft function beyond year 1.

CONCLUSIONS:

The findings of this study corroborate and augment data from previous registry surveys, and confirm the importance of observational studies in investigating the role of peritransplant parameters on long-term graft outcome.

121. Clin Transplant. 2005 Jun;19(3):391-8.

Risk factors for delayed kidney function and impact of delayed function on patient and graft survival in adult graft recipients.

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Acceso al artículo

Abstract

The influence of delayed kidney graft function on allograft outcome is described controversially in the literature. The aim of the study was to evaluate possible risk factors for delayed graft function (DGF) and investigate the impact of DGF on short- and long-term renal allograft function. Two groups were formed: the first one consisted of patients who gained immediate graft function (IGF) (n = 64) after transplantation and the second group included patients with DGF (n = 31; with at least one dialysis needed in first week after transplantation). The DGF group had a statistically significant longer duration on dialyses prior to transplantation (DGF 54 vs. IGF 33 months; $p < 0.05$), on average more frequently a re-transplantation (DGF 1.7 vs. IGF 1.3; $p < 0.01$), a longer re-anastomosis time (DGF 52.9 vs. 44.2 min; $p < 0.01$), a lower systolic (DGF 136 +/-24 mmHg vs. IGF 158 +/- 25; $p < 0.001$) and diastolic blood pressure (DGF 78 +/- 14 vs. IGF 89 +/- 16 mmHg; $p < 0.01$) at admission to the hospital and a higher serum (S)-creatinine at discharge (DGF 2.5 +/- 1.6 vs. IGF 1.6 +/- 0.4 mg/dL; $p < 0.01$). Prior to transplantation the DGF group had more often advanced vascular diseases (DGF 29.0 vs. IGF 12.5%; $p < 0.01$) and these patients incurred more frequently new ones during the next 3 yr after transplantation (DGF 22.6 vs. IGF 6.3%; $p < 0.001$). After 3 yr the graft survival tended to be lower in the DGF group (DGF 74.2 vs. IGF 84.4%; NS), but this difference was not statistically significant.

124. Transplant Proc. 2005 Apr;37(3):1431-2.

Similar impact of slow and delayed graft function on renal allograft outcome and function.

Rodrigo E[1], Fernández-Fresnedo G, Ruiz JC, Piñera C, Palomar R, González-Cotorruelo J, Zubimendi JA, De Francisco AL, Sanz de Castro S, Arias M.

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Acceso al artículo

Abstract

Kidney transplant patients can be divided into three groups, according to the initial graft function. First-week dialyzed patients form the delayed graft function (DGF) group. Nondialyzed patients are divided into slow graft function (SGF) or immediate graft function (IGF) according to whether the day 5 serum creatinine was higher versus lower than 3 mg/dL, respectively. SGF patients showed worse graft survival, above higher incidence of acute rejection and lower renal function than IGF patients, although few reports have analyzed outcomes in these groups. We analyzed the impact of SGF on graft survival, first-year renal function, and incidence of acute rejection in 291 renal transplant patients. Creatinine was significantly worse at 12 months for SGF and DGF than for IGF patients (1.9 +/- 0.8 mg/dL, 1.8 +/- 0.7 mg/dL, 1.5 +/- 0.5 mg/dL, respectively; $P < .05$). There was no difference in first-year renal function between SGF and DGF. The acute rejection rate was higher among the SGF than the IGF group (45% vs 21%, $P < .05$), but not different from DGF patients (42%, $P < .05$). Graft survival was better among IGF than SGF or DGF patients, with no significant difference between the last two groups (3-year graft survival, 82%, 71%, 70%, respectively; log-rank test, $P < .05$). Kidney transplant recipients who develop SGF have a worse outcome than patients with IGF, similar to DGF patients. SGF patients show worse graft survival, worse renal function, and higher acute rejection rates than IGF patients, despite not needing dialysis.

130. Curr Opin Crit Care. 2004 Dec;10(6):489-98.

Delayed graft function in renal transplantation.

Peeters P[1], Terryn W, Vanholder R, Lameire N.

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Abstract

PURPOSE OF REVIEW:

Delayed graft function is an important determinant of patient and graft survival. A complex of pathologic mechanisms intervenes in the pathophysiology of this outcome. This paper reviews the main processes involved in delayed graft function as they relate to five chronologically related stages: donor tissue quality, brain death and related stress, preservation variables, immune factors, and recipient variables.

RECENT FINDINGS:

Dialyzed delayed graft function and nondialyzed slow graft function both have a negative impact on graft survival and on the incidence of acute rejection. Expanded-criteria donors, older donors, and non-heart-beating donors are more frequently used. The long-term results of the use of well-selected non-heart-beating donors are surprisingly good. The process of ischemia/reperfusion injury is already initiated in the brain-death donor and continues during preservation of the graft. Graft-infiltrating T cells, heat shock proteins, and heme oxygenase-1 are implicated in the process. Modifications in immunosuppressive therapy and pharmacologic modulations have an effect on delayed graft function. Delayed graft function plays a part in the incidence of acute rejection, impaired graft function, and survival of patients and grafts.

SUMMARY:

This review discusses the current literature on several recent findings of pathophysiologic mechanisms of, and possible therapeutic interventions in, delayed graft function.

152. Ann Transplant, 2013; 18: 497-504

A retrospective analysis of long-term graft survival in 61 pediatric renal transplant recipients: A single-center experience

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Background:
Although short-term renal allograft survival in children has improved over the years, long-term graft outcomes remain unclear. In this study we report the characteristics and other variables that impact long-term kidney graft survival in children.

Material/Methods:
Records of 61 pediatric kidney transplant recipients (mean age: 14±3 years) performed at our institution between 1995 and 2011 were evaluated. Patients were divided into 2 groups (functional and non-functional grafts) to investigate the factors that impact graft survival. The groups were compared in terms of recipient characteristics, underlying disease, HLA status, immunosuppressive therapy, donor characteristics, acute rejection, and delayed graft function (DGF). Statistical significance was detected with the t and chi-squared tests (Pearson and Fisher's exact tests). Kaplan- Meier analysis was performed for graft survival.

Results:
Overall graft survival at 1, 5, 10, and 15 years were 93%, 66%, 46%, and 41%, respectively.
The median graft survival was 128.4 months (range: 3–188 months). Donor age, acute rejection, and DGF strongly predicted the chance of graft survival ($p<0.05$).

Conclusions:
It appears that several modifiable risk factors can partially account for poorer graft survival in pediatric kidney transplant recipients.

153. Kidney Int 2002; 62 (1):311
Postrasplant renal function in the first year predicts long term kidney
Hariharan s el al

155. Annual Transplant Report
NAPRTCS (2010)

Proyecto Prometeo II

Grupo I | Marcadores de supervivencia pretrasplante del donante y del receptor

Referencias Bibliográficas

Organizado por

SET
SOCIEDAD ESPAÑOLA DE TRASPLANTE

Con la colaboración de

NOVARTIS

1. Transplantation. 2014 Jan 15;97(1):64-70. doi: 10.1097/TP.0b013e3182a688a4.

Increased recipient body mass index is associated with acute rejection and other adverse outcomes after kidney transplantation.

Curran SP[1], Famure O, Li Y, Kim SJ.

Acceso al artículo

Abstract

BACKGROUND:

Outcomes of kidney transplant recipients with increased body mass index (BMI) remain controversial. We studied the relationship between BMI and clinically relevant outcomes among kidney transplant recipients at a large center.

METHODS:

We performed an observational cohort study of all recipients of kidney transplants at our center from January 1, 2000 to December 31, 2010 to determine if increased BMI at transplantation is associated with adverse outcomes, including delayed graft function and biopsy-proven acute rejection (BPAR). Recipient BMI was categorized as <20, 20 to 24.9 (reference), 25 to 29.9, 30 to 34.9, and ≥35 kg/m. Potential confounders were included in logistic and Cox proportional hazards models.

RESULTS:

A total of 1151 patients were studied. Recipient BMI of 30 to 34.9 and ≥35 kg/m were associated with an increased risk of delayed graft function (odds ratio [95% confidence interval [CI], 1.92 [1.16-3.19] and 4.49 [2.24-9.00], respectively). BMI≥35 kg/m was also associated with an increased risk of BPAR (hazard ratio [HR; 95% CI], 2.43 [1.48-3.99]), all-cause graft failure (HR [95% CI], 1.97 [1.09-3.56]), and death-censored graft failure (HR [95% CI], 2.43 [1.07-5.51]). Adjustment for acute rejection as a time-varying covariate significantly attenuated the association with graft failure endpoints. There was no significant relation between BMI and death with graft function.

CONCLUSIONS:

Increased BMI at kidney transplantation is a predictor of adverse outcomes, including BPAR. The role of pretransplantation weight reduction in improving graft and patient outcomes requires further study.

2. Transplantation. 2013 Nov 15;96(9):807-13. doi: 10.1097/TP.0b013e3182a0f668.

Pretransplantation erythropoiesis-stimulating agent hyporesponsiveness is associated with increased kidney allograft failure and mortality.

Costa NA[1], Kshirsagar AV, Wang L, Detwiler RK, Brookhart MA.

Acceso al artículo

Abstract

BACKGROUND:

Poor response to erythropoiesis-stimulating agents (ESA) is associated with morbidity and mortality among dialysis patients. It is unclear whether the risk associated with poor ESA response during dialysis extends beyond kidney transplantation. We examined pretransplantation ESA response and its effect on allograft failure and mortality.

METHODS:

The cohort included all adult Medicare recipients from the U.S. Renal Data System who had received a kidney transplant during years 2000 to 2007 and had at least 6 months of hemodialysis immediately before transplantation. ESA hyporesponsiveness was primarily defined as a monthly ESA dose of 75,000 units or higher and hematocrit 33% or less for at least 3 consecutive months in the pretransplantation period. Crude and adjusted Cox proportional hazards models and Kaplan-Meier methods were used to estimate the effect of ESA hyporesponsiveness on allograft failure and all-cause mortality.

RESULTS:

The study group consisted of 36,450 patients; 1004 exhibited hyporesponsiveness. The adjusted hazard ratios (95% confidence interval) for allograft failure and mortality after transplantation were 1.23 (1.10-1.42) and 1.61 (1.43-1.81), respectively, supporting that poor ESA response during hemodialysis is associated with adverse posttransplantation outcomes.

CONCLUSIONS:

ESA hyporesponsiveness may be useful in identifying potential allograft recipients who are at high risk for subsequent morbidity and mortality and may benefit from more intensive pretransplantation and posttransplantation monitoring.

3. Transplant Proc. 2012 Nov;44(9):2579-81. doi: 10.1016/j.transproceed.2012.09.086.
Cardiovascular risk in recipients with kidney transplants from expanded criteria donors.
Blanca L[1], Jiménez T, Cabello M, Sola E, Gutierrez C, Burgos D, Lopez V, Hernandez D.

Acceso al artículo

Abstract
INTRODUCTION:
Posttransplant cardiovascular disease (CVD) is the leading cause of death in renal transplant (RT) recipients and is more evident in recipients with transplants from expanded criteria donors (ECD).
OBJECTIVES:
We analyzed the evolution of cardiovascular risk factors and their association with patient mortality.
MATERIALS AND METHODS:
We undertook a single-center, prospective study of RT patients (n = 360) between 1999 and 2006. These were 180 recipients with transplants from ECD and 180 controls. We analyzed the baseline characteristics and the cardiovascular risk factors: hypertension, diabetes, dyslipidemia, CVD, and anemia. Posttransplant analyses included the evolution of cardiovascular risk factors and causes of death.
RESULTS:
The mean age of the ECD was 63.5 ± 5.4 versus 32.0 ± 13.2 years in the non-ECD (P < .001) and the recipient ages were 58.4 ± 8.7 versus 40.8 ± 13.3 years, respectively (P < .001). The median interquartile range [IQR] dialysis time was 25 months (15-39) versus 20 months (12-44; P = .017). The pretransplant body mass index was 26.89 ± 3.91 versus 25.43 ± 4.72 kg/m(2) (P = .002); the median (IQR) number of antihypertensive drugs was two (1-2) versus two (1-2.75; P = .015); dyslipidemia was present in 32.5% versus 21.6% (P = .024), diabetes in 10.6% versus 5.6% (P = .087), and CVD in 13.3% versus 7.8% (P = .086). Treatment with erythropoiesis-stimulating agents (ESA) was received by 84.9% versus 83.9% (P = .857). Concerning transplantation, the mean follow-up was 64.3 ± 33.7 months. Hypertension was present at 3 and 5 years in 85.6% versus 69.5% (P = .001) and 87.9% versus 72.8% (P = .009), respiratory. Treatment with angiotensin-converting enzyme inhibitors/angiotensin-II receptor blockers at 3 and 5 years was 79.8% versus 64.5% and 85.6% versus 65%. Dyslipidemia was present at 5 years in 63.1% versus 58.0% (P = .482). De novo diabetes occurred in 16.7% versus 11.1% (P = .128), and CVD in 13.5% versus 4.5% (P = .003). Univariate and multivariate Cox regression proportional hazards models were constructed to analyze the factors associated with patient death.
CONCLUSIONS:
CVD is the most common cause of death in recipients of ECD, RT, 40% in the ECD group versus 28.6% in the control group. Tight control of cardiovascular risk factors and a good pretransplant patient selection contributed to the good results obtained.

4. Transplant Proc. 2012 Nov;44(9):2529-31. doi: 10.1016/j.transproceed.2012.09.102.

Pretransplant donor-specific HLA antibodies detected by single antigen bead flow cytometry: risk factors and outcomes after kidney transplantation.

Kanter Berga J[1], Sancho Calabuig A, Gavela Martinez E, Puig Alcaraz N, Beltran Catalan S, Avila Bernabeu A, Crespo Albiach J, Montoro JA, Pallardo Mateu LM.

Acceso al artículo

Abstract

BACKGROUND:

The clinical significance of pretransplant donor-specific antibodies (pre-Tx DSAs) detected by single antigen bead flow cytometry (SAB-FC) remains unclear. Our aim was to investigate the impact that pre-Tx DSAs detected by SAB-FC have on the early and late clinical outcomes.

PATIENTS AND METHODS:

We retrospectively tested stored frozen pre-Tx sera from 222 deceased-donor kidney transplants performed between November 1997 and November 2006. All patients had a negative complement-dependent cytotoxicity (CDC) cross-match with the donor. Median follow up was 5.1 years.

RESULTS:

Twenty-two (10%) patients had pre-Tx HLA antibodies detected by CDC. Pre-Tx HLA antibodies were detected using SAB-FC in the sera of 46 (20.7%) patients; 36 (16.2%) of them presented pre-Tx DSAs, 18 had class I antibodies, 9 class II, and 9 patients presented both classes. Mean pre-Tx DSA class I/II was 2360/1972 (MFI) mean fluorescence index in non CDC-sensitized patients. Pre-Tx DSAs were associated with female sex, retransplants, and pretransplant transfusions. Patients with Pre-Tx DSAs more than 1000 MFI and negative CDC screening presented a higher percentage of delayed graft function (61.1% versus 38.9%), more episodes of acute vascular rejection (33.3% versus 13.7%), and chronic rejection as the cause of allograft failure (22.2% versus 9.7%) compared with non-pre-Tx DSAs patients. Five-year allograft survival was significantly worse in patients with pre-Tx DSA (68.5% versus 82%, P = .006) and in patients with pre-Tx DSA class II more than 1000 MFI (43% versus 82%, P = .009). We didn't find differences in patient survival.

DISCUSSION:

Pre-Tx DSAs detected by SAB-FC were more frequent in female recipients, and they were associated with acute vascular and chronic rejection and a poorer graft outcome.

5. Nephrol Dial Transplant. 2012 Aug;27(8):3345-51. doi: 10.1093/ndt/gfs064. Epub 2012 Apr 12.

Association of pre-transplant erythropoiesis-stimulating agent responsiveness with post-transplant outcomes.

Molnar MZ[1], Bunnapradist S, Huang E, Krishnan M, Nissenson AR, Kovesdy CP, Kalantar-Zadeh K.

Acceso al artículo

Abstract

BACKGROUND:

The role of pre-transplant erythropoiesis-stimulating agent (ESA) responsiveness in affecting post-transplant outcomes is not clear.

METHODS:

Linking the 5-year patient data of a large dialysis organization to the 'Scientific Registry of Transplant Recipients', we identified 8795 hemodialyzed patients who underwent first kidney transplantation. Mortality or graft failure, delayed graft function (DGF) and acute rejection risks were estimated by Cox regression [hazard ratio (HR)] and logistic regression, respectively.

RESULTS:

Patients were 48 ± 14 years old and included 38% women and 36% diabetics. Compared to renal allograft recipients who were in the first quartile of pre-transplant ESA responsiveness index (ERI), i.e. ESA dose divided by hemoglobin and weight, recipients in second, third and fourth quartiles had higher adjusted graft-censored death HR (and 95% confidence intervals) of 1.7 (1.0-2.7), 1.8 (1.1-2.9) and 2.3 (1.4-3.9) and higher death-censored graft failure HR of 1.6 (1.0-2.5), 2.0 (1.2-3.1) and 1.6 (0.9-2.6), respectively. No significant association between pre-transplant ERI and post-transplant DGF or acute rejection was detected.

CONCLUSIONS:

Higher pre-transplant ERI during the hemodialysis treatment period was associated with worse post-transplant long-term outcomes including increased all-cause death and higher risk of graft failure.

6. Clin J Am Soc Nephrol. 2011 Nov;6(11):2712-21. doi: 10.2215/CJN.06190611. Epub 2011 Sep 29.

Association of pretransplant serum phosphorus with posttransplant outcomes.

Sampaio MS[1], Molnar MZ, Kovesdy CP, Mehrotra R, Mucsi I, Sim JJ, Krishnan M, Nissenson AR, Kalantar-Zadeh K.

Author information:
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Comment in

- Transplantation: Pretransplantation serum phosphorus level: association with mortality and graft survival. [Nat Rev Nephrol. 2011]

Acceso al artículo

Abstract

BACKGROUND AND OBJECTIVES:

Serum phosphorus levels are associated with mortality, cardiovascular disease, and renal function loss in individuals with and without chronic kidney disease. The association of pretransplant serum phosphorus levels with transplant outcomes is not clear.

DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS:

Data of the Scientific Registry of Transplant Recipients (SRTR) up to June 2007 were linked to the database (2001 through 2006) of one of the U.S.-based large dialysis organizations (DaVita). The selected 9384 primary kidney recipients were divided into five groups according to pretransplant serum phosphorus levels (mg/dl): <3.5, 3.5 to <5.5 (reference group), 5.5 to <7.5, 7.5 to <9.5, and ≥9.5. Unadjusted and multivariate adjusted risks for transplant outcomes were compared.

RESULTS:

Patients were 48 ± 14 years old and included 37% women and 27% African Americans. After multivariate adjustment, all-cause and cardiovascular death hazard ratios were 2.44 (95% confidence interval: 1.28 to 4.65) and 3.63 (1.13 to 11.64), respectively, in recipients in the ≥9.5 group; allograft loss hazard ratios were 1.42 (1.04 to 1.95) and 2.36 (1.33 to 4.17) in recipients with 7.5 to >9.5 and ≥9.5, respectively. No significant association with delayed graft function was found.

CONCLUSIONS:

Pretransplant phosphorus levels 7.5 to <9.5 mg/dl and ≥9.5 mg/dl were associated with increased risk of functional graft failure and increased risk of all-cause and cardiovascular deaths, respectively, when compared with 3.5 to <5.5 mg/dl. Additional studies are needed to examine whether more aggressive control of pretransplant serum phosphorus may improve posttransplant outcomes.

PMCID: PMC3359573 **Free PMC Article**

7. Clin Transplant. 2011 Jul-Aug;25(4):E437-46. doi: 10.1111/j.1399-0012.2011.01461.x. Epub 2011 Apr 25.

Hypertension in standard criteria deceased donors is associated with inferior outcomes following kidney transplantation.

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Acceso al artículo

Abstract

BACKGROUND:

Hypertension may be a either a cause or an effect of kidney disease. Although hypertension is an important component of the expanded criteria donor definition, risks of transplanting deceased donor kidneys from hypertensive standard criteria donors (SCD) are less well understood.

METHODS:

Retrospective single-center study in all adult patients who received a deceased donor kidney transplant from a SCD to evaluate the role of donor hypertension as a pre-transplant risk factor for death-censored graft loss (DCGL) and renal function.

RESULTS:

From October 2001 through May 2008, 297 kidney transplants were performed from donation after brain death SCDs. A total of 47 (15.8%) grafts were lost, including 19 (6.4%) deaths with functioning grafts. Univariate analysis of death-censored cases (n = 278) identified history of donor hypertension, cold ischemia time (CIT) >30 h, and African American (AA) recipients as significant pre-transplant risk factors predictive for DCGL at five yr follow-up (mean 38 months, all $p < 0.02$). Cox regression analysis showed donor hypertension (relative risk 2.2, $p = 0.04$) to be a significant risk factor for DCGL, whereas CIT >30 h and AA recipient ethnicity showed only trends toward DCGL. Renal function as determined by serum creatinine levels was significantly higher in recipients of hypertensive compared with non-hypertensive SCD kidneys at all time points out to 48 months follow-up and the disparity in renal function increased over time.

CONCLUSIONS:

Transplanting SCD kidneys from hypertensive donors is associated with worse graft function and an increased risk of graft loss.

8. Clin J Am Soc Nephrol. 2011 Jun;6(6):1481-7. doi: 10.2215/CJN.09201010. Epub 2011 May 12.
Impact of pre-existing hepatitis B infection on the outcomes of kidney transplant recipients in the United States.

Reddy PN[1], Sampaio MS, Kuo HT, Martin P, Bunnapradist S.

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Acceso al atículo

Abstract
BACKGROUND AND OBJECTIVES:
Pre-existing hepatitis B virus (HBV) infection has been associated in inferior renal transplant outcomes. We examined outcomes of HBV+ renal recipients in a more recent era with availability of oral anti-viral agents.
DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS:
Using the Organ Procurement Transplant Network/United Network for Organ Sharing database, we selected adult primary kidney recipients transplanted in the United States (2001 to 2007). The cohort was divided into HBV+ (surface antigen positive, n = 1346) and HBV- patients (surface antigen negative; n = 74,335). Five-year graft survival, patient survival, hepatic failure incidence, and associated adjusted risks were compared.
RESULTS:
HBV+ recipients were more frequently Asian, had a lower body mass index, and glomerulonephritis was more prevalent as the etiology of ESRD. HBV+ recipients had less pretransplant diabetes and cardiovascular disease, were less likely a living donor recipient, and were less likely to receive steroids at discharge. Five-year patient survival was 85.3% and 85.6% and graft survival was 74.9% and 75.1% for HBV+ and HBV-, respectively. HBV infection was not a risk factor for death or kidney failure, although 5-year cumulative incidence of hepatic failure was higher in HBV+ recipients (1.3% versus 0.2%; $P < 0.001$), and HBV+ was associated with 5.5- and 5.2-fold increased risk for hepatic failure in living and deceased donors, respectively, compared with HBV-.
CONCLUSIONS:
In a recent era (2001 to 2007), HBV-infected renal recipients were not at higher risk for kidney failure or death; however, they remain at higher risk of liver failure compared with HBV- recipients.
PMCID: PMC3109947 **Free PMC Article**

9. Transplantation. 2011 Apr 27;91(8):869-74. doi: 10.1097/TP.0b013e3182100f3a.
Effect of obesity on the outcome of kidney transplantation: a 20-year follow-up.

Hoogeveen EK[1], Aalten J, Rothman KJ, Roodnat JI, Mallat MJ, Borm G, Weimar W, Hoitsma AJ, de Fijter JW.

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Comment in

- Re: effect of obesity on the outcome of kidney transplantation: a 20-year follow-up. [J Urol. 2012]

Acceso al artículo

Abstract

BACKGROUND:

Cardiovascular disease is both a major threat to the life expectancy of kidney transplant recipients and an important determinant of late allograft loss. Obesity is an important risk factor for cardiovascular disease.

METHODS:

We investigated the relation between both pretransplant and 1-year posttransplant body mass index (BMI) with patient and renal graft survival in a cohort of 1810 adult patients. Sixty-one percent of all patients were men; median age (interquartile range [IQR]) was 46 years (35-56 years); median (IQR) pretransplant BMI was 23.0 kg/m (20.8-25.6 kg/m); 1 year after transplantation, the median (IQR) BMI had increased 1.6 kg/m (0.3-3.2 kg/m) and median (IQR) follow-up time was 8.3 years (5.3-12.0 years). We categorized BMI as follows: less than or equal to 20, more than 20 to less than or equal to 25 (normal), more than 25 to less than or equal to 30, and more than 30 (obesity) kg/m.

RESULTS:

Using a Cox proportional hazards model, after adjustment for cardiovascular risk factors, the relative risks (95% confidence intervals) of death and death-censored graft failure during all follow-up for pretransplant obesity compared with normal BMI were 1.22 (0.86-1.74) and 1.34 (1.02-1.77), respectively; for obesity 1 year after transplantation compared with normal BMI, it was 1.39 (1.05-1.86) and 1.39 (1.10-1.74), respectively; and for change in BMI (per 5 kg/m increment) during the first year after transplantation, it was 1.23 (1.01-1.50) and 1.18 (1.01-1.38), respectively.

CONCLUSIONS:

One year posttransplant BMI and BMI increment are more strongly related to death and graft failure than pretransplant BMI among kidney transplant recipients. Patients with BMI more than 30 kg/m compared with a normal BMI have approximately 20% to 40% higher risk for death and graft failure.

10. Am J Kidney Dis. 2010 Dec;56(6):1127-39. doi: 10.1053/j.ajkd.2010.06.027. Epub 2010 Oct 8.
Associations of pretransplant diabetes mellitus, new-onset diabetes after transplant, and acute rejection with transplant outcomes: an analysis of the Organ Procurement and Transplant Network/United Network for Organ Sharing (OPTN/UNOS) database.

Kuo HT[1], Sampaio MS, Vincenti F, Bunnapradist S.

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Comment in

- The tradeoff between the risks of acute rejection and new-onset diabetes after kidney transplant. [Am J Kidney Dis. 2010]

Acceso al artículo

Abstract

BACKGROUND:

Diabetes and acute rejection are major contributors to morbidity and mortality in kidney transplant recipients. Immunosuppressive medications decrease acute rejection, but increase the frequency of new-onset diabetes after transplant. Our objective was to investigate the joint associations of diabetes (pretransplant diabetes and new-onset diabetes after transplant) and acute rejection with transplant outcomes in a recent transplant cohort.

STUDY DESIGN:

Historical cohort study.

SETTING & PARTICIPANTS:

37,448 recipients (age ≥ 18 years; 2004-2007) surviving with a functioning transplant for longer than 1 year were identified in the Organ Procurement and Transplant Network/United Network for Organ Sharing (OPTN/UNOS) database as of May 22, 2009.

PREDICTORS:

Recipients were stratified into 6 mutually exclusive groups according to status of diabetes and acute rejection at 1 year: group 1, neither (reference; n = 20,964); group 2, new-onset diabetes alone (n = 2,140); group 3, pretransplant diabetes alone (n = 10,730); group 4, acute rejection alone (n = 2,282); group 5, new-onset diabetes and acute rejection (n = 361); and group 6, pretransplant diabetes and acute rejection (n = 1,061). Analyses were adjusted for other recipient, donor, and transplant characteristics. OUTCOMES MEASUREMENTS: Multivariate Cox regression analysis of time to transplant failure (overall and death censored) and mortality (all-cause and cardiovascular).

RESULTS:

Median follow-up after 1 year was 548 days (25th-75th percentiles, 334-752 days). During this time, there were 3,047 outcomes of overall transplant failure. New-onset diabetes alone (group 2) was not associated significantly with any study outcomes. Groups 3-6 were associated with higher overall transplant failure risk. However, only groups 4-6 were associated with higher death-censored transplant failure risk. Group 3, 4, and 6 were associated with higher all-cause mortality risk, whereas only groups 3 and 6 were associated with higher cardiovascular mortality risk.

LIMITATIONS:

Potential information bias with exposure, covariable, or outcome misclassification; relatively short follow-up.

CONCLUSIONS:

Pretransplant diabetes is the major predictor of all-cause and cardiovascular mortality, and acute rejection during the first year is the major predictor of death-censored transplant failure in kidney recipients surviving with a functioning transplant for at least 1 year. The influence of new-onset diabetes on long-term outcomes needs further observation.

11. Transplantation. 2010 Nov 27;90(10):1079-84. doi: 10.1097/TP.0b013e3181f6a07b.

Pretransplant donor-specific antibodies detected by single-antigen bead flow cytometry are associated with inferior kidney transplant outcomes.

Singh N[1], Djamali A, Lorentzen D, Pirsch JD, Leverson G, Neidlinger N, Voss B, Torrealba JR, Hofmann RM, Odorico J, Fernandez LA, Sollinger HW, Samaniego M.

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Acceso al artículo

Abstract

BACKGROUND:

The clinical significance of pretransplant donor-specific antibodies (pre-Tx DSAs) detected by single-antigen bead flow cytometry (SAB-FC) remains unclear.

METHODS:

To investigate the impact that pre-Tx DSAs detected by SAB-FC have on early clinical outcomes, we tested pre-Tx sera from all consecutive deceased-donor kidney transplants performed between January 2005 and July 2006 (n=237).

RESULTS:

In the study population of which 66% had a high-immunologic risk, mean fluorescence intensity (MFI) more than or equal to 100 for class I and more than or equal to 200 for class II were the lowest DSA thresholds associated with inferior antibody-mediated rejection-free graft survival (75% vs. 90%, P=0.004 and 76% vs. 87%, P=0.017, respectively). The hazard ratio for antibody-mediated rejection increased linearly with higher class II DSA from MFI 100 to 800 (1.7[0.8-3.2], P=0.1 for MFI ≥100 vs. 4.7[2.4-8.8], P<0.001 for MFI ≥ 800). Differences in graft function were only evident in patients with class II MFI more than or equal to 500 (estimated glomerular filtration rate: 47.6 vs. 54.3, P=0.02 and proteinuria: 0.6 ± 0.6 vs. 0.4 ± 0.3, P=0.03). A difference in death-censored graft survival was detected in patients with class II MFI more than or equal to 1000 (75% vs. 91.9%, P=0.055).

CONCLUSION:

High-pre-Tx DSAs detected by SAB-FC are associated with incrementally poor graft outcomes in deceased-donor kidney transplant with high-immunologic risk.

12. Transplant Proc. 2010 Nov;42(9):3497-502. doi: 10.1016/j.transproceed.2010.09.009.
Clinical outcome of preemptive kidney transplantation in patients with diabetes mellitus.
Son YK[1], Oh JS, Kim SM, Jeon JM, Shin YH, Kim JK.

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Acceso al artículo

Abstract
End-stage renal disease (ESRD) caused by diabetic nephropathy is increasing throughout the world. The survival of diabetic patients treated by transplantation has improved nowadays. Although recent studies have demonstrated preemptive kidney transplantation to be associated with better graft survival in CKD patients, the effect of pre-transplantation dialysis on graft outcomes among diabetic ESRD patients is unclear. This analysis summarized our experience with preemptive kidney transplantation in diabetic ESRD patients by retrospectively comparing 70 such patients transplanted between 1995 and 2009. These 70 patients were divided into two groups: 30 patients underwent preemptive and the other 40 transplantation after maintenance hemodialysis or peritoneal dialysis. We compared graft survivals, acute rejection episodes, postoperative complications, and delayed graft function rates. The 10-year patient survival of 100% in the preemptive group was similar to that of the nonpreemptive group (85%, P = .11). But the 10 year graft survival was higher among the preemptive than the nonpreemptive group (100% vs 75%, P = .02). Pre-transplantation modality did not affect graft survival. Therefore, preemptive kidney transplantation should be applied to eligible patients with diabetic ESRD.

13. Clin Nephrol. 2009 Jul;72(1):62-8.

Influence of dialysis modality on renal transplant complications and outcomes.

Yang Q[1], Zhao S, Chen W, Mao H, Huang F, Zheng Z, Chen L, Fei J, Yu X.

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Abstract

AIMS:

The present study investigated the influence of the pretransplant dialysis modality, hemodialysis (HD) or peritoneal dialysis (PD), on renal transplant complications and outcomes.

METHODS:

402 cadaveric renal transplant patients maintained on HD (N = 303) or PD (N = 99) for more than 3 months prior to transplantation were studied retrospectively, and a total of 345 patients were followed up for 30.2 +/- 15.2 months. The impact of HD or PD on acute rejection, delayed graft function (DGF), infection, chronic rejection, and the survival rate of graft and patients were analyzed.

RESULTS:

There was no significant difference between the HD and PD groups with regard to the causes of end-stage renal disease, age, gender, blood pressure, hemoglobin, HLA match, hot and cold ischemia time, and hepatitis C virus infection. The incidence rates of DGF, acute rejection, chronic rejection and cytomegalovirus and other infections were also not significantly different between the HD and PD groups. However, compared to HD, patients with PD had longer dialysis duration ($p < 0.05$), but less hepatitis B infection ($p < 0.05$) and post-transplant infection ($p < 0.05$). In contrast, in those PD patients with hepatitis B infection, graft loss was significantly increased (19.23% vs. 8.86% , $p = 0.021$). The incidence of acute rejection episodes was higher in HD patients who had pretransplant dialysis for more than 12 months ($p < 0.05$). The overall patient and graft survival rates within 5 years between the HD and PD groups were not significantly different ($p > 0.05$).

CONCLUSIONS:

The influence of PD and HD on complications after renal transplant at 1 year and 5 years and graft survival rates was similar, and therefore, either HD or PD can be chosen as the pretransplant dialysis modality. However, patients in the PD group had a reduced incidence of hepatitis virus infection, suggesting that PD may have certain advantages over HD as a preoperative substitution therapy for renal transplantation.

14. Transpl Int. 2008 Oct;21(10):985-91. doi: 10.1111/j.1432-2277.2008.00717.x. Epub 2008 Jun 28.

Associations between pre-kidney-transplant risk factors and post-transplant cardiovascular events and death.

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Acceso al artículo

Abstract

The prevalence of cardiovascular risk factors in renal transplant candidates is high. A better understanding of the relation between these risk factors and cardiovascular morbidity and mortality is mandatory to improve transplantation outcome. In this retrospective cohort study 2187 adult patients who received a first kidney transplant between 1984 and 1997 were included. We analyzed the incidence of post-transplant cardiovascular events and tried to identify independent pretransplant risk factors for post-transplant cardiovascular events and all-cause mortality. The cumulative incidence of post-transplant cardiovascular events was 40%. The incidence was highest in the first 3 months after transplantation. Independent pretransplant risk factors for a post-transplant cardiovascular event were diabetic nephropathy [Hazard ratio (HR) 3.02; 95% CI 2.85-3.98], claudication [HR 2.17 (1.42-3.31)], cardiac event [HR 1.76 (1.32-2.33)], cerebrovascular accident HR 1.53 (1.03-2.28), time-on-dialysis [HR 1.06 (1.02-1.11)], recipient age [HR 1.04 (1.04-1.05)], and body mass index [HR 1.03 (1.00-1.05)]. Diabetic nephropathy and cardiovascular disease were also important predictors for all-cause mortality. Diabetic nephropathy and cardiovascular disease were the most important predictors for cardiovascular events and all-cause mortality after renal transplantation. Early treatment of cardiovascular risk factors and pretransplant cardiovascular evaluation might improve transplantation outcome.

15. Clin Transplant. 2007 Sep-Oct;21(5):609-14.

Renal transplant outcome in high-cardiovascular risk recipients.

Jeloka TK[1], Ross H, Smith R, Huang M, Fenton S, Cattran D, Schiff J, Cardella C, Cole E.

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Acceso al artículo

Abstract

BACKGROUND:

Cardiovascular (CV) disease is the foremost cause of mortality and an important cause of morbidity in renal transplant recipients. The disease burden is likely to increase as older patients are accepted for transplantation. The outcome of these high-CV risk patients after renal transplantation, especially with known pre-transplant coronary artery disease (CAD), has not been studied. Hence, we looked at the CV outcome in patients with known pre-transplant CAD.

METHODS:

All renal transplants performed between 1998 and 2002 at our center, followed up to 2005, were divided into high- and low-risk groups, based on the presence of one or more of the following: pre-transplant angina, myocardial infarction, and positive coronary angiogram. The two groups were compared for post-transplant cardiac events and patient and graft survival. The factors predictive of post-transplant cardiac events were also determined by Cox-regression multivariate analysis.

RESULTS:

Forty-five patients (10.5%), out of 429, had post-transplant cardiac events; 31.3% in the high risk, and 6.5% in the low-risk group (p = 0.001). Five-yr patient survival was lower in the high-risk group (82.8% vs. 93.1%, p = 0.004), while five-yr overall graft survival and death censored graft survival were statistically not different (74.8% vs. 84.1%, p = 0.08 and 87.3% vs. 90%, p = 0.25). Forty-one percent of patients who were treated with angioplasty plus stenting or bypass graft prior to transplantation had post-transplant cardiac events, as compared with 28% of those without intervention in the high-risk group and 6.5% of patients in the low-risk group (p = 0.001). Age, pre-transplant cardiac disease, arrhythmias, and low-ejection fraction (< or = 40%) were significant independent predictors of post-transplant cardiac events.

CONCLUSION:

Post-transplant survival of high-CV risk patients (with known CAD) is lower than that of low-risk recipients but remains acceptable. Cardiac interventions may reduce perioperative risk but do not reduce the probability of post-transplant cardiac events to that of low-risk group.

16. Am J Transplant. 2007 Mar;7(3):550-9. Epub 2006 Dec 6.

A "weight-listing" paradox for candidates of renal transplantation?

Schold JD[1], Srinivas TR, Guerra G, Reed AI, Johnson RJ, Weiner ID, Oberbauer R, Harman JS, Hemming AW, Meier-Kriesche HU.

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Comment in

- Lack of interventional studies in renal transplant candidates with elevated cardiovascular risk. [Am J Transplant. 2007]

Acceso al artículo

Abstract

Research suggests that end-stage renal disease patients with elevated body mass index (BMI) have superior outcomes on dialysis. In contrast, low and high BMI patients represent the highest risk cohorts for kidney transplant recipients. The important question remains concerning how to manage transplant candidates given the potentially incommensurate impact of BMI by treatment modality. We conducted a retrospective analysis of waitlisted and transplanted patients in the United States from 1990 to 2003. We constructed Cox models to evaluate the effect of BMI on mortality of waitlisted candidates and identified risk factors for rapid weight change. We then assessed the impact of weight change during waitlisting on transplant outcomes. Decline in BMI on the waiting list was not protective for posttransplant mortality or graft loss across BMI strata. Substantial weight loss pretransplantation was associated with rapid gain posttransplantation. The highest risk for death was among listed patients with low BMI (13-20 kg/m(2), adjusted hazard ratio = 1.47, $p < 0.01$). Approximately one-third of candidates had a change in BMI category prior to transplantation. While observed declines in BMI may be volitional or markers of disease processes, there is no evidence that candidates have improved transplant outcomes attributable to weight loss. Prospective trials are needed to evaluate the efficacy of weight loss protocols for candidates of kidney transplantation.

Free Article

17. J Am Soc Nephrol. 2005 Feb;16(2):496-506. Epub 2004 Dec 22.

Incidence and predictors of myocardial infarction after kidney transplantation.

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Acceso al artículo

Abstract

The risk and predictors of post-kidney transplantation myocardial infarction (PTMI) are not well described. Registry data collected by the United States Renal Data System were used to investigate retrospectively PTMI among adult first renal allograft recipients who received a transplant in 1995 to 2000 and had Medicare as the primary payer. PTMI events were ascertained from billing and death records, and participants were followed for up to 3 yr after transplant or until the end of observation (December 31, 2000). Extended Cox's hazards analysis was used to identify independent clinical correlates of PTMI (hazard ratio [HR]) and to examine PTMI as an outcomes predictor. Among 35,847 eligible participants, the cumulative incidence of PTMI was 4.3% (95% confidence interval [CI], 4.1 to 4.5%), 5.6% (95% CI, 5.3 to 5.8%), and 11.1% (95% CI, 10.7 to 11.5%) at 6, 12, and 36 mo, respectively. Risk factors for PTMI included older recipient age, pretransplantation comorbidities (diabetes, angina, peripheral vascular disease, and MI), transplantation from older donors and deceased donors, and delayed graft function. Women, blacks, Hispanics, and employed recipients experienced reduced risk. The hazard of PTMI rose after a diagnosis of posttransplantation diabetes (HR, 1.60; 95% CI, 1.35 to 1.88) and markedly increased after graft failure (HR, 2.78; 95% CI, 2.41 to 3.19). In separate analyses, PTMI predicted death-censored graft failure (HR, 1.89; 95% CI, 1.63 to 2.20) and strongly predicted death in a manner that declined with time after PTMI. Risk factors for PTMI include potentially modifiable posttransplantation complications. Because PTMI in turn predicts graft failure and death, reducing the risk for PTMI may improve outcomes after kidney transplantation.

Free Article

18. Clin Transplant. 2004 Oct;18(5):619-23.

Renal transplantation offers a better survival in HCV-infected ESRD patients.

Sezer S[1], Ozdemir FN, Akcay A, Arat Z, Boyacioglu S, Haberal M.

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Acceso al artículo

Abstract

Sezer S, Ozdemir FN, Akcay A, Arat Z, Boyacioglu S, Haberal M. Renal transplantation offers a better survival in HCV-infected ESRD patients. Clin Transplant 2004 DOI: 10.1111/j.1399-0012.2004.00252. Abstract: The presence of hepatitis C virus (HCV) infection has been found to adversely affect the morbidity and mortality rates in the dialysis population. Renal transplantation is a treatment option after a careful pre-transplant evaluation. We designed this study to find the impact of HCV infection on patient survival, co-morbidity and allograft survival in a selected group of hemodialysis (HD) and transplant population. We retrospectively analyzed 116 renal transplant patients (94 HCV-negative, 22 HCV-positive) and 136 HD patients (106 HCV-negative, 30 HCV-positive) who had renal transplantation or underwent dialysis before 1996. The HCV-infected patients were evaluated by liver biopsy for the absence of advanced liver disease before transplantation. There was no clinical or laboratory decompensation of liver disease in transplant and dialysis patient groups. The overall 5-yr survival rates were 85.2% for renal transplant recipients and 74.5% for those on HD. The comparison results revealed a significant difference between HCV-infected patients with and without transplantation. The 3-yr renal allograft survival rates were comparable in HCV-positive and -negative patients, but the risk of chronic allograft nephropathy (CAN) and graft failure were higher at the fifth year in HCV-positive patients. In conclusion, renal transplantation should the preferred therapy in HCV-infected dialysis patients as it improves the survival rates. The presence of HCV infection increases the CAN rate and the influence on allograft survival is evident at the fifth year of assessment.

19. Clin Transpl. 2004:303-14.

Explainable variation in renal transplant outcomes: a comparison of standard and expanded criteria donors.

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Abstract

In 2002, OPTN/UNOS altered kidney allocation rules to allow patients to be listed separately to receive kidneys from expanded criteria donors (ECD). Our aim was to quantify the short- and long-term impacts of 21 prognostic factors on recipients of ECD as well as recipients of living (LD) and deceased standard criteria (SCD) donors. A factor's impact depends on both the risk and diversity of its effects. Using OPTN/UNOS Registry data from 1996-2003, we have analyzed kidney-only, adult-recipient grafts for factor effects among 35,878 LD, 47,941 SCD and 10,399 ECD transplants. During an early risk period, all 94,218 recipients were followed through one year, and, in the late risk period, 85,270 recipients whose grafts survived beyond one year were followed for 5 years post-transplant. Impact was measured by determining a factor's percentage of assignable variation in one- and 5-year graft failure rates. Scores for 21 factors were estimated via generalized logistic models, which contained a random component for transplant center. The assignable variation associated with a given factor was computed as the factor score variance multiplied by the square of the corresponding regression coefficient. Impacts were heterogeneous with regard to posttransplant period and donor type. The top 5 factors influencing one-year graft survival rates were as follows: * For LD grafts - pretransplant dialysis time (14% of the variation in short-term outcomes), recipient age (13%), body mass (12%), PRA (10%) and induction therapy (10%). * For SCD grafts - donor age (24%), recipient age (12%), pretransplant dialysis time (12%), HLA-DR matching (6%) and pretransplant medical condition (6%). * For ECD grafts - donor age (18%), pre-transplant dialysis time (10%), recipient age (10%), pretransplant medical condition (10%) and recipient body mass (6%). Ranking long-term outcomes demonstrated the following top 5 influential factors: * For LD grafts - donor age (28% of the variation in long-term outcomes), recipient race (15%), age (15%), transplant year (13%) and recipient sex (11%). * For SCD grafts - donor age (35%), recipient race (23%), transplant year(15%), recipient sex (8%)and age (5%). * For ECD grafts - donor age (33%), recipient sex (20%), race (15%), transplant year (8%) and recipient's original disease (5%). Donor age was the dominant factor governing the survival rates among deceased donor kidney transplants. Advancing donor age was still the major risk factor for SCD transplant failure despite setting aside all donors 60 and up, and a large fraction of 50-59 year-old donors, from this group. Current ECD/SCD definitions warrant review and possible revision.

20. Kidney Int. 2002 Nov;62(5):1848-54.
Risk factors for late kidney allograft failure.
Ponticelli C[1], Villa M, Cesana B, Montagnino G, Tarantino A.

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[1]Divisione di Nefrologia e Dialisi, and Epidemiologic Unit, IRCCS Ospedale Maggiore Milano, Milano, Italy.
Comment in

- Risk factors for late kidney allograft failure. [Kidney Int. 2003]

Acceso al artículo

Abstract
BACKGROUND:
While graft survival rates in the short term have improved dramatically, only a modest improvement has been shown in long-term graft survival rates. We evaluated the causes of late failure in renal allograft recipients treated with cyclosporine A (CsA).
METHODS:
A total of 864 adults with a functioning graft at one year were evaluated. The end points were dialysis or death with a functioning graft.
RESULTS:
The 13-year patient and graft survival probabilities were 0.82 and 0.64, respectively. The graft half-life was 20.1 years and the pure graft half-life was 31.1 years. At multivariate analysis, plasma creatinine at one year (P = 0.0006; RR 1.72), low-density lipoproteins (LDL) at one year (P = 0.0014; RR 1.65), older age (P = 0.0128; RR 1.50) and delayed graft function (P = 0.0350; RR 1.45) were associated with the end point. Chronic allograft nephropathy was the cause of failure in 97 patients, death in 70, recurrence of glomerulonephritis in 24, other events in 6. Cardiovascular complications were the most frequent cause of death. Post-transplant cardiovascular events were associated with: pre-transplant cardiovascular events (P = 0.0012; RR 2.65), older age (P = 0.0001; RR 2.46), pre-transplant arterial hypertension (P = 0.0249; RR 1.57), smoking (P = 0.0235; RR 1.29), duration of dialysis (P = 0.0229; RR 1.28). Mean serum cholesterol, LDL and triglycerides were each significantly associated post-transplant cardiovascular events.
CONCLUSIONS:
The graft half-life was 20 years. Chronic allograft nephropathy was the leading cause of late failure, followed by death. If the data were censored by death, the projected pure graft half-life would be 31.1 years. Pre-transplant selection and preparation of the candidate as well as appropriate life style are recommended to improve life expectancy and extend graft survival.
Free Article

21. Int Urol Nephrol. 2014 Apr;46(4):825-32. doi: 10.1007/s11255-013-0521-0. Epub 2013 Sep 8.

Pretransplant peritoneal dialysis relative to hemodialysis improves long-term survival of kidney transplant patients: a single-center observational study.

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BACKGROUND:
Kidney transplantation is the best option for the treatment of end-stage renal disease in terms of survival and quality of life. These results can be influenced by the pretransplant dialysis modality. The aim of this study was to evaluate whether the pretransplantation dialysis modality influences patient and allograft survival beyond 10 years and examine the potential risk
factors associated with the outcomes.
METHODS:
We conducted an observational, retrospective, single-center clinical study that included 236 patients [118 undergoing peritoneal dialysis (PD) and 118 undergoing hemodialysis (HD)] who proceeded to transplantation during the period December 1990-2002. Donor and recipient data were collected from our hospital's clinical registries. The follow-up period extended to the patient's death, the loss of the allograft, or loss to follow-up. The end date of the study was set at March 2012.
RESULTS:
In the multivariate analysis, the long-term patient survival rate was higher for the PD group than for the HD group [HR = 2.62 (1.01-6.8); p = 0.04]; however, the allograft survival rate was not significantly different between the two groups [HR = 0.68 (0.41-1.10); p = 0.12].
CONCLUSION:
Pretransplantation dialysis modality is associated with long-term patient survival, with outcomes favoring peritoneal dialysis over hemodialysis.However, the pretransplant dialysis modality does not influence long-term graft loss risk.

22. Transplantation. 2014 Feb 27;97(4):426-32.

Pre-implant biopsy predicts outcome of single-kidney transplantation independent of clinical donor variables.

Hofer J(1), Regele H, Böhmig GA, Gutjahr G, Kikić Z, Mühlbacher F, Kletzmayr J.

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Division of Nephrology and Dialysis, Department of Medicine III, Medical University of Vienna, Vienna, Austria. 4 Competence Centre for Clinical Trials, University of Bremen, Bremen, Germany. 5 Department of Surgery, Medical University of Vienna, Vienna, Austria. 6 Department of Medicine III, SMZ-Ost/Donauspital, Vienna, Austria. 7 Address correspondence to: Josef Kletzmayr, M.D., Department of Medicine III, SMZ-Ost/Donauspital, Langobardenstrasse 122, 1220 Vienna, Austria.

BACKGROUND:
Pre-implant biopsy findings account for the discard of many donor kidneys although their clinical value is not fully understood. We retrospectively investigated the predictive value of pre-implant histology, which in our center was obtained for protocol purposes, not for transplant decisions, on long-term allograft and recipient outcome after single-kidney transplantation.
METHODS:
This single-center study included 628 consecutive adult recipients of 174 Expanded Criteria Donor (ECD) and 454 Standard Criteria Donor kidneys.
Chronic donor organ injury was assessed applying a chronic lesion score differentiating between mild, moderate, and severe histologic organ injury based on the integration of glomerular, vascular, tubular, and interstitial lesions.
Recipients were followed over a median time of 7.8 years.
RESULTS:
Donor kidneys exhibiting mild or moderate chronic lesions yielded almost identical graft and recipient survival independent of ECD status or other clinical covariables (HR 1.20, 95% CI 0.83-1.74, P=0.326, and HR 1.27, 95% CI 0.83-1.95, P=0.274, respectively). However, if allograft injury was severe, occurring in 3% of transplanted kidneys, graft and recipient survival was significantly reduced (HR 3.13, 95% CI 1.61-6.07, P<0.001 and HR 2.42, 95% CI 1.16-5.04, P=0.005, respectively).
CONCLUSION: The results suggest that donor kidneys displaying moderate chronic injury can safely be transplanted as single kidneys, while organs displaying severe injury should be discarded. Thus, pre-implant biopsy might offer an effective approach to increase the utilization of renal donor organs, especially from ECD and donors with cerebrovascular accident as cause of death, and to improve overall graft outcome.

23. Transplant Proc. 2013 Oct;45(8):2907-13.

Implication of donor-recipient age gradient in the prognosis of graft outcome after deceased-donor kidney transplantation.

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PURPOSE:
Successful kidney transplantation leads to greater survival and improved quality of life for patients with end-stage renal disease. Among the most important influences on graft outcomes is donor age. We evaluated the relationships between the donor-recipient age gradient (DRAG) and the graft outcomes after deceased-donor kidney transplantation (DDKT).
METHODS:
From February 1995 to March 2011, a consecutive series of 526 adult DDKT recipients were analyzed. DRAG values were divided into two groups (negative versus positive years) and then four groups (≤-21, -20 to -1, 0 to 20, and ≥21 years).
RESULTS:
Median age of donors and recipients were 39 (range, 1-75) and 41 (range, 18-74) years, respectively. The degree of DRAG was not associated with episodes of allograft rejection. High or low DRAG had no effect on posttransplant serum creatinine levels or estimated glomerular filtration rates. However, negative levels of DRAG, particularly less than -20 years, were significantly correlated with superior 10-year death-censored graft survival (86.4% and 83.1% vs 72.2% vs 53.9%; overall P = .031), but not increased overall graft or patient survival.
CONCLUSION: This study demonstrated that DRAG is a prognostic indicator of long-term graft outcomes after DDKT.

24. J Am Soc Nephrol. 2012 Nov;23(11):1891-9.

Donor ABCB1 variant associates with increased risk for kidney allograft failure.

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The impact of variation within genes responsible for the disposition and metabolism of calcineurin inhibitors (CNIs) on clinical outcomes in kidney transplantation is not well understood. Furthermore, the potential influence of donor, rather than recipient, genotypes on clinical endpoints is unknown. Here, we investigated the associations between donor and recipient gene variants with outcome among 4471 white, CNI-treated kidney transplant recipients. We tested for 52 single-nucleotide polymorphisms (SNPs) across five genes: CYP3A4, CYP3A5, ABCB1 (MDR1; encoding P-glycoprotein), NR1I2 (encoding the pregnane X receptor), and PPIA (encoding cyclophilin). In a discovery cohort of 811 patients from Birmingham, United Kingdom, kidney donor CC genotype at C3435T (rs1045642) within ABCB1, a variant known to alter protein expression, was associated with an increased risk for long-term graft failure compared with non-CC genotype (hazard ratio [HR], 1.69; 95% confidence interval [CI], 1.20-2.40; P=0.003). No other donor or recipient SNPs were associated with graft survival or mortality. We validated this association in 675 donors from Belfast, United Kingdom (HR, 1.68; 95% CI, 1.21-2.32; P=0.002), and in 2985 donors from the Collaborative Transplant Study (HR, 1.84; 95% CI, 1.08-3.13; P=0.006). In conclusion, these data suggest that an ABCB1 variant known to alter protein expression represents an attractive candidate for future study and risk stratification in kidney transplantation.

25. Transplantation. 2010 Oct 27;90(8):867-74.

Long-term impact of donor-recipient size mismatching in deceased donor kidney transplantation and in expanded criteria donor recipients.

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BACKGROUND:
The degree to which recipient/donor (R/D) size mismatching leads to nephron underdosing and worse kidney allograft survival remains poorly defined, particularly in the setting of preexisting nephron loss such as the expanded criteria donor (ECD).
METHODS:
We performed a retrospective analysis of 69,737 deceased donor transplants followed by a subset analysis of ECD transplants using data from the Scientific Registry of Transplant Recipients from 1992 to 2005. Ratios of R/D body surface area (BSA) were used to estimate nephron disparity and segregate pairs.
RESULTS:
In the entire cohort, severe BSA disparity (R/D BSA>1.38 m) was associated with slightly worse 10-year unadjusted graft survival (35% for severe BSA disparity vs. 39% in pairs of comparable size, P<0.0001). In multivariate analysis, BSA disparity was associated with a 15% increased risk of graft loss (hazard ratio 1.15, P<0.0001). Within ECD cohorts, severe BSA disparity was associated with a decrease in 10-year unadjusted graft survival of greater magnitude than the overall cohort (10% for severe BSA disparity vs. 22% in pairs of comparable size, P<0.0004). On multivariate analysis, severe R/D BSA disparity was associated with worse allograft survival similar to the entire cohort (hazard ratio 1.18, P=0.04).
CONCLUSIONS:
Recipients receiving kidneys from substantially smaller donors have a statistically higher rate of graft loss that is more pronounced in ECD kidneys.
Although severe R/D size disparity is an independent risk factor for graft loss, the magnitude of this risk requires consideration in the context of other risk factors for the graft loss and the hazards of dialysis.

26. Pediatr Nephrol. 2008 Nov;23(11):2075-9.

Study of the effect of donor source on graft and patient survival in pediatric renal transplant recipients.

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Comment in
Pediatr Nephrol. 2009 Jul;24(7):1425; author reply 1427.

Evaluation of the impact of live unrelated kidney donor (LURD) source on the outcome of renal transplantation is not adequately studied. We aimed to compare the long-term outcome of kidney transplantation from LURDs to that from living related donors (LRDs) among a pediatric recipient population. This study comprised 235 pediatric recipients who received their kidney grafts between 1976 and 2005 at our center. These patients were further subdivided into two groups according to donor source (211 with LRDs) and (24 with LURDs). All patients' data were assessed with special emphasis on graft and patient survival as well as posttransplant medical complications. Both groups were comparable regarding graft and patient survival at 1, 5, and 10 years. Despite higher incidence of acute vascular rejection among recipients with LURD (12%) vs. LRD (2.8%) (P = 0.03), there was no difference in the incidence of chronic allograft nephropathy. Moreover, the overall incidence of posttransplant complications was comparable among the two groups. In our series, kidney survival was poorer in LURDs compared with LRDs. However, the number of patients with LURD was small, and the difference in results was also small and justifies LURD in exceptional cases when LRD is not possible.

27. Transplant Proc. 2007 Sep;39(7):2123-4.

Preemptive kidney transplant from deceased donors: an advantage in relation to reduced waiting list.

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BACKGROUND:
Preemptive living donor kidney transplantation is associated with better allograft and recipient survival. However, it remains unclear whether preemptive transplantation from deceased donors is beneficial too. An increased number of deceased donors has reduced the waiting list in our hospital in the last year allowing preemptive deceased donor kidney transplantation (PDDKT).
AIM:
We compared our experience with preemptive transplantation with patients who underwent dialysis before transplantation.
PATIENTS AND METHODS:
Thirty-three PDDKT, including 77.5% male patients of overall mean age of 48 +/- 14 years, were performed in our hospital between January 1999 and December 2004 (8% of transplantations). We compared the outcomes of these patients with those of renal transplants in subjects who had undergone dialysis. The donors for both groups had similar characteristic; they were paired donor kidneys in most cases.
RESULTS:
The types of donors in both groups were: non-heart-beating (49%), heart-beating deceased (27%) or en bloc pediatric (24%). The serum creatinine of the recipients was 6.9 +/- 1.8 mg/dL prior to transplantation, and the creatinine clearance was 14.6 +/- 3.6 mL/min (estimated by the Cockroft-Gault formula). The Charlson comorbidity index adapted for patients with advanced chronic kidney disease (ACKD) was 0.8 +/- 0.2 in the preemptive group versus 1.7 +/- 0.4 in the dialysis group ($P < .05$). Delayed graft function rates were 0% versus 25% in preemptive vs dialysis groups, respectively. No differences in 1-month or 1-year renal function as determined by serum creatinine were observed between the groups. We did not observe differences in the incidence of acute rejection or 1- and 2-year graft and patient survivals.
CONCLUSION:
PDDKT is the treatment of choice for ACKD. It is associated with less delayed graft function and similar 2-year graft and patient survivals than kidney transplantation after dialysis. The Charlson index reflected less comorbidity among patients with PDDKT, a finding that must influence long-term outcomes.

28. Transplant Proc. 2005 Nov;37(9):3716-7.

Association of the genetic polymorphisms of the renin-angiotensin system with kidney graft long-term outcome: preliminary results.

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Recent studies have demonstrated some association between the renin-angiotensin system (RAS) activity and the development and progression of different entities as diabetes mellitus (DM) or chronic allograft nephropathy. To investigate these associations, we studied some gene polymorphisms of RAS in a group of renal transplant recipients. We retrospectively analyzed 42 patients who underwent a primary renal transplantation for 2 years. A subgroup of 23 patients (55%) was diagnosed with postransplant DM in accordance with American Diabetes Association 2001 criteria. We studied two RAS gene polymorphisms: the angiotensin-converting enzyme insertion/deletion (ACE I/D) and angiotensinogen (AGTM235T). Genotyping was performed by DNA purification and amplification with a polymerase chain reaction technique. The distributions of genotypes were ACE DD, ID, II: 33%, 48%, 19%; and AGT TT, MT, MM: 15%, 45%, 40%, respectively. We observed a progressive loss in renal function measured by creatinine clearance (Cockroft) in D-allele carriers (DD+ID) between the first and the second transplantation year: 65.3 +/- 4.3 vs 59.8 +/- 4.6 mL/min (P = 0.02); that was not seen in II patients: 68.8 +/- 4.6 vs 68.4 +/- 4 mL/min (P = 0.87). Fifty percent of D-allele carriers developed DM vs 25% of non-D-allele carriers (P = 0.19). Eighty-three percent of homozygous patients for the AGT-TT allele developed DM vs 35% of non TT patients (P = 0.04).
There were no significant differences regarding recipient demographic characteristics, type of donor, number and severity of acute rejections, and immunosuppressant treatment between the groups. In conclusion, ACE D-allele seems to be associated with a poorer kidney graft long-term outcome. ACE D and AGT T alleles may be implicated in glucose metabolism disorders after transplantation.

29. Transplantation. 2005 Aug 27;80(4):466-70.

Risk factors for short- and long-term survival of primary cadaveric renal allografts in pediatric recipients: a UNOS analysis.

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BACKGROUND:
Pediatric kidney graft survival rates have improved in the United States. This study evaluates early and late risk factors for cadaveric graft loss in pediatric recipients.
METHODS:
From January 1994 to December 2002, 2,597 primary cadaveric kidney-alone transplants (donor age 5-45 years, recipient age 2-20 years) were reported to the United Network for Organ Sharing (UNOS). The analysis includes follow-up information based on OPTN data as of October 14, 2003. Odds ratio of early graft loss and relative risk of late graft loss are estimated using logistic regression and Cox proportional hazards model, respectively.
RESULTS:
Graft survival rates significantly improved during 1999-2002 (95% and 79% at 1-year and 3-years, respectively) compared with those of 1994-1998 (88% and 76% at 1-year and 3-years, respectively) (log rank P=0.02). After adjusting for other variables, the factors that significantly affected early transplant outcome adversely within 3 months posttransplant were prolonged cold ischemia time (>36 hours, odds ratio [OR]=3.38 vs. 0-36 hours) and young recipient age (2-5 years old, OR=2.02 vs. 6-12 years). Beyond 3 months, significant risk factors were African-American recipients (relative risk [RR]=1.93 vs. others), teenage recipients (13-20 yrs, RR=1.50 vs. 6-12 yrs), and patients with focal glomerulosclerosis (FGS) (RR=1.27 vs. others).
CONCLUSIONS:
The short-term graft survival rate of pediatric cadaveric kidney transplants has significantly improved, yet the long-term outcome has changed little. The long-term outcomes for teenagers (13-20 yrs), patients with FGS, and African-Americans lag significantly behind other groups. In order to improve long-term graft survival in these high-risk patients, newer preventive or treatment strategies must be developed.

30. Transplant Proc. 2004 Sep;36(7):2040-2.

The impact of sex and age matching for long-term graft survival in living donor renal transplantation.

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BACKGROUND:

Deficient functional renal mass leads to progressive renal injury owing to the detrimental effects of glomerular hyperfiltration. Therefore, renal transplant mass is an important determinant of outcome.

MATERIALS AND METHODS:

We retrospectively analyzed 614 living donor renal transplantations performed from 1979 to 2002. Patients were divided into 4 groups according to donor-recipient gender differences: group 1 (male to male), group 2 (male to female), group 3 (female to male), and group 4 (female to female). We analyzed the clinical and immunological data to compare the 4 groups with respect to long-term graft survival, age gender, acute rejection episodes an HLA matching. We used the Kaplan-Meier method with the log-rank test to assess graft survival.

RESULTS:

The actuarial graft survival rate was 86.24% at 5 years for donors younger than 50 years of age compared with 73.15% for those older than 50 years (P = .0000). The graft survival from younger donors than recipients was 85.23% at 5 years compared with 80.35% for older donors (P = .0213). The graft survival of group 3 (female donor to male recipient) was 75.12% at 5 years compared with 85.72%, 85.33%, and 83.16% for groups 1, 2, and 4, respectively (P = .0165). The main parameters significantly associated with graft survival were donor age (P = .0000), acute rejection episode (P = .0000), donor gender (P = .0215). HLA-DR matching (P = .0516), and donor and recipient age matching (P = .0213).

CONCLUSIONS:

The results suggest that the sex and age matching between donors and recipients should be considered as a criterion in the choice of donor and recipient pairs for living donor renal transplantation.

31. Nephrol Dial Transplant. 2005 Jan;20(1):167-75. Epub 2004 Nov 16.
Duration of end-stage renal disease and kidney transplant outcome.
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BACKGROUND:
Patients nearing end-stage renal disease (ESRD) increasingly choose pre-emptive renal transplant (PRT) to avoid pre-transplant dialysis and to minimize ESRD. Compared with long-term dialysis, PRT has been shown to increase allograft survival. However, the merit of short-term dialysis is not well characterized, and it may be the better medical choice in some patients. The goal of the study was to characterize the relationship between the duration of dialysis vs allograft and patient survival.
METHODS:
We performed a retrospective nationwide cohort study of all kidney transplants (Tx) between January 1, 1990 and December 31, 1999, with a follow-up period through December 31, 2000. Participants were identified using the United States Renal Data System (USRDS), which tracks all ESRD cases in the nation including patients on dialysis and with kidney Tx. Patients with the history of more than one kidney Tx were excluded. Allograft survival and recipient survival were the primary outcomes of this study. Duration of ESRD as a continuous variable as well as divided into categories (14 days, 15-60 days, 61-180 days, 181-365 days, 1-2 years, 2-3 years, 3-5 years and >5 years) was the primary risk factor of interest. Models were adjusted for multiple donor and recipient factors, including demographics and co-morbidities, as well as for Tx procedure characteristics.
RESULTS:
A total of 81,130 patient records were used for analysis (age 44.1+/-14.3 years, 61% males, 24% black, 29% diabetic, pre-transplant ESRD duration 27.1+/-26.4 months, 26% living donors). ESRD duration, as a continuous variable, is associated with a modest increase in the risk of graft failure over time [hazard ratio (HR) 1.02 per year of ESRD duration, P<0.001]. When ESRD is studied as a categorical variable (duration of 0-14 days vs longer durations), the increased risk of allograft failure reached statistical significance only when the time on dialysis was > or =181 days. The duration of ESRD was a significant risk for recipient death (HR 1.04 per year, P<0.001); however, mortality risk reached statistical significance only when the patient had been on dialysis for > or =1 year.
CONCLUSIONS:
This study of USRDS records suggests that a short (<6 months) dialysis course has no detrimental effect on graft and patient survival, and should not be deferred if medically indicated.

32. Am J Nephrol. 2003 Sep-Oct;23(5):294-9. Epub 2003 Aug 6.

Effect of donor/recipient body weight mismatch on patient and graft outcome in living-donor kidney transplantation.

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BACKGROUND/AIMS:
There have been conflicting reports showing that kidneys from small donors may be at risk for graft loss if they are transplanted into large recipients. The aim of this work was to examine the donor/recipient body weight ratio (D/RBWR) on patient and graft outcome.
METHODS:
During the period from January 1990 to January 2002, 856 kidney transplants were performed. Of these, 776 kidney transplant recipients were selected after exclusion of pediatric, second transplant patients and those with a body mass index of 35. All patients achieved a minimum follow-up of 1-year.
According to D/RBWR, patients were divided into 3 groups: low (0.9), medium (0.91-1.2) and high (1.2). Data were collected on graft function, acute and chronic rejection, post-transplant complications, and 1- and 5-year graft and patient survival.
RESULTS:
There was a statistically significant increase in the incidence of chronic rejection, post-transplant hypertension and diabetes mellitus in the low group. The incidence and frequency of acute rejection episodes were nearly the same in the 3 groups. Graft function, estimated by serum creatinine at 1 year, was significantly lower in the low group. The 5-year graft and patient survival was 71, 80, 88 and 81, 85 and 92%, in the low, medium and high groups, respectively.
CONCLUSIONS:
We conclude that a low D/RBWR may contribute to inferior long-term renal allograft survival. The hyperfiltration hypothesis due to low nephron mass in the low D/RBWR group may explain these findings.

33. Transplantation. 2002 Sep 15;74(5):664-9.

Long-term renal function in kidneys from non-heart-beating donors: A single-center experience.

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BACKGROUND: Cadaveric kidneys from brain-stem-dead donors continue to be limited because the number of donors has reached a plateau. Wide recruitment of non-heart-beating donors (NHBD) could significantly increase the donor pool. NHBD renal transplants are underused because of the concern of poor quality graft function from such donors. In response to this perception, we reviewed 46 NHBD renal transplants performed in our center since 1998.
METHODS: All NHBD kidneys were machine-perfused using the Newcastle continuous-hypothermic pulsatile preservation system before transplantation. A control heart-beating-donor (HBD) group was taken as the next consecutive HBD renal transplant to the NHBD transplant. The outcome and quality of function of the groups of renal transplants were analyzed for short-term and long-term performance.
RESULTS: The renal transplant patients were matched for donor and recipient factors. Survival rates for allografts and patients were similar for 1 to 3 years. There was an increased incidence of delayed graft function in the NHBD renal transplants in the perioperative period. The creatinine clearance was 22.8+/-2.3 mL/minute for NHBD patients and 44.4+/-2.9 mL/minute for HBD patients at the time of discharge from hospital. This difference equalized after 3 months and the creatinine clearance for NHBD was 44.2+/-2.4 mL/minute and for HBD 49.2+/-3.4 mL/minute.
CONCLUSIONS: Our results for NHBD renal transplants confirm that such grafts suffer primary warm ischemic injury, shown by the increased incidence of acute tubular necrosis and consequent delayed graft function. This produced poor renal function at the time of hospital discharge. After 3 months, the renal function of NHBD cases improved to the level seen in HBD patients.

34. Transplantation. 2002 Apr 15;73(7):1095-9.
Graft survival and graft function of pediatric en bloc kidneys in paraaortal position.

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Comment in
Transplantation. 2003 Jun 27;75(12):2158-9.

BACKGROUND:
En bloc kidneys from pediatric donors are regarded as questionable with respect to the safety and quality of the transplant outcome. Therefore, we retrospectively studied graft outcome and graft function of our 56 en bloc kidneys transplanted in paraaortal position between 1992 and 1999.
METHODS:
Graft outcome of en bloc kidneys (group A) was compared with graft outcome of single cadaveric adult donor kidneys (group B). Matched pairs were generated regarding HLA-missmatch, cold ischemic time, recipient age, body mass index, and systolic arterial blood pressure.
RESULTS:
Allograft survival rates of pediatric en bloc kidneys at 1, 3, and 5 years were significantly lower (group A: 78, 70, 70% vs. group B: 92, 92, 81%, $P<0.05$). Lower survival rate was caused by a higher number of graft losses in the early postoperative period (group A: 21% vs. group B: 4%, $P<0.01$) due to vascular complications. Main risk factor for graft loss was donor age of less than 12 months. Five years after transplantation serum creatinine of pediatric en bloc kidneys was significantly better than of adult kidneys (0.9+/-0.06 vs. 1.8+/-0.2 mg/dl, $P<0.001$).
CONCLUSION:
En bloc kidneys show a high percentage of graft survival with excellent long-term graft function. However, the early postoperative period carries a higher risk of graft loss in very young donors due to vascular complications. In the face of donor shortage en bloc kidneys from pediatric donors can successfully be transplanted in a paraaortal position.

35. Transplantation. 2001 Sep 15;72(5):940-7.

Time-dependent risk factors influencing the long-term outcome in living renal allografts: donor age is a crucial risk factor for long-term graft survival more than 5 years after transplantation.

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BACKGROUND:
Most investigations have revealed that the improvement in early graft survival has not resulted in a corresponding improvement in long-term graft survival. The risk factors for long-term graft survival should be clarified.
METHODS:
A single-center experience of 1100 consecutive renal transplant recipients who received kidneys from living donors from 1983 to 1998 was reviewed to clarify the time dependency of risk factors for long-term graft survival. We examined various possible risk factors, including HLA-AB and -DR mismatches, ABO-blood group incompatibility, graft weight, donor age and sex, recipient age and sex, and the presence or absence of acute rejection by using the time-dependent, nonproportional Cox's hazards model.
RESULTS:
Acute rejection episode, donor age, HLA-AB 4-antigen mismatches, ABO-incompatible transplantation, smaller kidney weight compared with the patient's body weight (Kw/Bw ratio less than 2.67), and transplantation from an unrelated living donor were risk factors for long-term graft outcome.
Multivariate analysis for time-dependent risk factors showed that donor age of more than 60 years was the most important risk factor for long-term graft failure after 5 years posttransplantation (hazard ratio: 2.57). In contrast, acute rejection, ABO incompatibility, and nonrelated donors were significant risk factors for short-term graft failure within 5 years after kidney transplantation (hazard ratios: 2.68, 1.57, and 1.69, respectively).
CONCLUSIONS:
Donor age of more than 60 years was a crucial risk factor affecting long-term graft survival. In contrast, acute rejection, ABO incompatibility, and nonrelated donors were significant risk factors for short-term graft failure.

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Proyecto Prometeo II

Grupo III

Inmunosupresión y función renal a largo plazo: hay evidencias?

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Organizado por

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Con la colaboración de

NOVARTIS

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Factors influencing long-term outcome after kidney transplantation.
Legendre C[1], Canaud G, Martinez F.

Author information:
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Acceso al artículo

Abstract
Many factors influence the long-term outcome of kidney transplantation, which is defined very schematically by patient death or renal dysfunction leading to graft loss. The most important of these factors is most likely the quality of the transplant itself, with kidneys from living donors showing a positive impact, while kidneys from expanded criteria donors show deleterious impacts. Various clinicopathological scores exist to predict mid- to long-term outcomes and avoid the transplantation of kidneys displaying inferior results. The key factors related to the recipient include their age as well as disease recurrence, HLA matching, HLA immunization, ethnic background, time on dialysis, and cardiovascular comorbidities. Renal function, defined based on estimated GFR and/or proteinuria values, is a result of all these factors. Delayed graft function has a detrimental long-term impact, as does the level of renal function impairment either in stable condition or in case of progressing dysfunction. Finally, although current immunosuppression regimes are highly efficient in preventing acute rejection, the burden of specific (diabetes, nephrotoxicity) and nonspecific (infection and cancer) side effects has significant negative long-term consequences that may well be worse in the future because of the increasing ages of both donors and recipients. The development of safer immunosuppression strategies is therefore crucial to improve long-term outcomes.

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Chronic allograft dysfunction: major contributing factors.
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Acceso al artículo

Abstract
Chronic, progressive, and irreversible loss of a transplanted kidney function, previously named chronic allograft nephropathy, is the leading cause of chronic allograft failure among kidney transplant recipients. Chronic allograft dysfunction (CAD) is a multifactorial process associated with progressive interstitial fibrosis and tubular atrophy. Current Data confirms that an additive series of time-dependent immunological factors such as acute and chronic antibody- and/or cell-mediated rejection and nonimmunological factors are involved in development of interstitial fibrosis and tubular atrophy as the fundamental parts of CAD. The use of calcineurin inhibitors has produced a major impact on achieving successful organ transplantation; however, although this assumption has been doubted recently, calcineurin inhibitors are deemed to be associated with nephrotoxicity and subsequent interstitial fibrosis, tubular atrophy, and kidney dysfunction. The early fibrotic changes are due to implantation stress, T-cell-mediated rejection, and infection; however, usually they do not lead to progressive fibrosis and allograft dysfunction per se. In the setting of CAD, many factors occurring lately after 1 year, such as chronic antibody-mediated rejection, recurrent or de novo glomerulonephritis, and nonadherent adequately address the existence of ongoing injuries and progression to fibrosis. Identification of patients who are at risk, close clinical monitoring, and optimization and individualization of their maintenance immunosuppressive regimen are among the means that could help us to improve the long-term outcome of kidney transplantation.
Free Article

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Long-term outcome of ATG vs. Basiliximab induction.

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Acceso al artículo

Abstract

BACKGROUND:

An evaluation of the long-term efficacy and incidence of adverse events after induction therapy with antithymocyte globulin (ATG) vs. Basiliximab in renal transplant patients.

METHODS:

Sixty recipients receiving ATG induction and a dual immunosuppression with Tacrolimus and steroids were compared retrospectively with 60 patients treated with Basiliximab. The following characteristics were evaluated: concomitant immunosuppression, recipient age, donor age, time on dialysis, cold ischemia time, year of transplantation and HLA mismatches.

RESULTS:

The 6-year patient survival in the ATG group was 91·7% compared to 85% in the Basiliximab group (not significant, n.s.). Graft survival at 6 years was 89·7% and. 83·6% in the ATG and the Basiliximab group (n.s.), respectively. Incidence of biopsy proven acute rejection episodes (33·3% vs. 26·7%) and delayed graft function (30% vs. 33·3%) were similar in both groups. Kidney function was not significantly different at 1 and 6 years. CMV infections were more prevalent in the ATG arm (22% vs. 5%; P = 0·05), and a significantly higher rate of haematological complications was observed following ATG induction.

CONCLUSIONS:

ATG induction was associated with an improved (but n.s.) trend in patient and graft survival. Patients induced with ATG had a higher rate of CMV infections and haematological complications.

4. Transplant Proc. 2009 Nov;41(9):3690-2. doi: 10.1016/j.transproceed.2009.06.197.

Long-term experience of plasmapheresis in antibody-mediated rejection in renal transplantation.

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Acceso al artículo

Abstract

BACKGROUND:

Antibody-mediated rejection (AMR) continues to pose a serious challenge in renal transplantation with potentially devastating consequences. Treatment options for this condition include plasmapheresis, high-dose intravenous immunoglobulin (IVIG), plasmapheresis with low-dose IVIG, and the use of rituximab (anti-CD20 chimeric antibody). We previously reported on the short-term outcome of plasmapheresis as a rescue therapy for AMR in our centre. We now report on the long-term follow up.

METHODS:

Over a 2.5-year study period, 440 cadaveric transplants were performed. AMR developed in 20 (4.5%) patients. Treatment included plasmapheresis and intensification of their immunosuppressive therapy.

RESULTS:

Excluding two patients who had infarcted their grafts at diagnosis, 18 patients received plasmapheresis treatment for AMR. Of the 18 patients treated, 14 recovered function, two developed graft infarction within a fortnight of starting plasmapheresis, and two patients were withdrawn from treatment. In the 14 who recovered renal function, graft survival was 86% at 12 months. In this study we report on the 5-year follow-up of these AMR-treatment responders. Eleven patients have a functioning graft at 5 years; graft function was stable with a mean serum creatinine of 130 micromol/L at 5 years compared to 123 mumol/L at 1 year. At 5-years follow-up; graft survival was 78% and patient survival 93%.

CONCLUSIONS:

Little information is available in the literature regarding the long-term outcome of this therapy. This is the first report on the long-term (5-year) follow-up of plasmapheresis as a rescue therapy for AMR.

5. Transplantation. 2009 Jun 27;87(12):1821-9. doi: 10.1097/TP.0b013e3181a66cfc.

Calcineurin inhibitor-based immunosuppressive therapy, donor age, and long-term outcome after kidney transplantation.

Heinze G[1], Oberbauer R, Kainz A, Mitterbauer C, Koppelstaetter C, Hörl WH, Mayer G.

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Acceso al artículo

Abstract

BACKGROUND:

It is unclear whether the choice of maintenance immunosuppression modulates the negative effect of advanced donor age on outcome after renal transplantation.

METHODS:

All 1829 patients who received their first transplant between 1990 and 2003 at the Vienna Medical Centre and had a functioning graft after 90 days were studied. At this time point, 1587 received calcineurin inhibitors (CNI+), 242 did not (CNI-). Actual and functional graft survival was analyzed in subgroups based on donor age (<36, 36-49, 50-64, and >64 years) and immunosuppressive therapy.

RESULTS:

The median follow-up time was 7 years. In total, we observed 312 deaths and 275 graft losses. After adjusting for several variables considered as potential confounders, actual graft survival was better in CNI+ patients compared with CNI- patients only if donor age was less than 36 years (adjusted hazard ratio 0.25, 95% confidence interval 0.17-0.38) or 36 to 49 years (0.43, 95% confidence interval 0.29-0.62). Similar results were obtained for functional graft survival. Patient survival was significantly better in CNI+ subjects irrespective of donor age (0.41, 95% confidence interval 0.30-0.57).

DISCUSSION:

Use of CNI 90 days after transplantation is associated with improved patient survival even after adjustment for confounders, but its beneficial association with actual and functional graft survival is lost or at least reduced if kidneys from donors older than 50 years are used.

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Kidney transplantation: future challenges.
Veroux M[1], Corona D, Veroux P.

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Acceso al artículo

Abstract
Kidney transplantation is the best replacement therapy for the patients with end-stage renal disease, by offering an increased longevity and quality of life. However, the demand for kidney exceeds the available supply, so that the number of people on waiting list is steadily increasing. Many transplant centers have tried to supply to this chronic shortage of organs, by utilizing kidney from older donors or from donors with a previous hepatitis, and this strategy resulted in a safe way to increase the donor pool. Living transplantation has progressively increased in last years so that the number of living donors exceeds in the USA the deceased donors. Although one-year graft survival is excellent, long-term outcomes has not improved in last years. Death from cardiovascular disease, infection and malignancy are common complications of immunosuppression and are the leading causes of mortality in kidney transplant recipients. Viral infections and donor-transmitted infections will be probably the emerging challenge in the next years. Physicians must be aware in developing newer immunosuppressive regimens, with lower side effects, which may improve the long-term outcome of kidney transplantation. Reduction of death with functioning graft and chronic allograft nephropathy will be the greatest challenge of all physicians who care for kidney transplant recipients.

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Evaluation of two different preconditioning regimens for ABO-incompatible living kidney donor transplantation. A comparison of splenectomy vs. rituximab-treated non-splenectomy preconditioning regimens.

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Acceso al artículo

Abstract

INTRODUCTION:

Although splenectomy has been employed in most documented protocols for ABO-incompatible kidney transplantation (ABO-ILKT), its utility is not yet determined. The aim of this study was to evaluate the long-term results of ABO-ILKT with splenectomy, and also compare the outcome of ABO-ILKT with splenectomy versus non-splenectomy.

METHODS:

We did a retrospective study of ABO-incompatible living donor kidney transplants at our institution and affiliated hospital between January 2001 and December 2006 (n = 70). All patients were treated with a combination of immunosuppressive drugs, including tacrolimus (FK), mycophenolate mofetil (MMF) and methylprednisolone (MP). Between January 2001 and December 2004, all patients underwent pretransplant double filtration plasmapheresis (DFPP) and splenectomy at the time of transplant (n = 46) (ABO-I-SPX group). Between January 2005 and December 2006, splenectomy was not performed and a protocol that involved pretransplant low-dose injection of rituximab was employed (ABO-I-RIT group). ABO-compatible living kidney transplants (n = 55) performed between January 2001 and December 2004 were employed as a control group (ABO-C group).

RESULTS:

Patient survival was 100% in all groups. Three-year graft survival was 98.2, 93.5 and 95.8% in the ABO-C, ABO-I-SPX and ABO-I-RIT groups, respectively. Five-year graft survival was 93 and 91.3% in the ABO-C and ABO-I-SPX groups, respectively. Renal allograft function was comparable among the three groups. However, compared to the ABO-I-RIT group, the incidence of acute antibody-mediated rejection (acute AMR) or chronic AMR was significantly higher in the ABO-C and ABO-I-SPX groups.

CONCLUSIONS:

Although long-term outcome of the ABO-I-SPX group was excellent and showed no significant difference compared to the ABO-C group, splenectomy is not essential for successful ABO-ILKT. The rituximab-treated patients showed excellent short-term graft survival and renal function, and the incidence of AMR in the ABO-I-RIT group was significantly reduced compared to the ABO-I-SPX group.

8. Am J Transplant. 2008 Mar;8(3):574-85. doi: 10.1111/j.1600-6143.2007.02099.x.

Long-term outcome of early steroid withdrawal after kidney transplantation in African American recipients monitored by surveillance biopsy.

Anil Kumar MS[1], Khan S, Ranganna K, Malat G, Sustento-Reodica N, Meyers WC.

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Acceso al artículo

Abstract

Generally chronic steroid therapy is standard care for African American (AA) kidney recipients because of their higher incidence of rejections and lower long-term graft survival. This prospective study evaluated the long-term safety and efficacy of early steroid withdrawal (ESW) in AA recipients. A total of 206 recipients were studied; 103 AA and 103 non-AA recipients monitored by serial surveillance biopsies from 1 to 60 months posttransplantation to evaluate subclinical acute rejections (SCAR) and chronic allograft injury (CAI). Biopsy-proven clinical acute rejections (BPAR) and SCAR were treated. Primary end point was BPAR and secondary end points were 5-year SCAR, CAI and survival. Incidences of BPAR was 16% versus 14% (p = 1.0), prevalence of CAI due to hypertension was 48% versus 30% (p = 0.05) and interstitial fibrosis/tubular atrophy was 47% versus 32% (p = 0.05) and the mean serum creatinine levels were 2.1 versus 1.8 mg/dL (p = 0.05) at 5-years in AA versus non-AA recipients. The incidence of SCAR was 23% versus 11% at 1 month (p = 0.04), 12% versus 3% at 3 years (p = 0.04) and 10% versus 1% at 5 years (p = 0.04) in AA and non-AA recipients, respectively. Five-year patient survivals were 81% and 88% (p = 0.09) and graft survivals were 71% and 73%(p = 0.19) in AA and non-AA groups, respectively. After early steroid withdrawal AA kidney recipients have significantly lower renal function and higher SCAR and CAI but 5-year graft survival are comparable to non-AA recipients.

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9. Langenbecks Arch Surg. 2007 Sep;392(5):511-23. Epub 2007 Apr 21.

Current concepts and perspectives of immunosuppression in organ transplantation.

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Acceso al artículo

Abstract

BACKGROUND:

While early surgical success made organ transplantation possible in the 1950s and 1960s, the breakthrough in clinical organ transplantation was achieved through the discovery and invention of modern immunosuppressive agents in the early/mid-1980s. Especially during the 1990 s, a large array of immunosuppressants has expanded the armamentarium used to prevent and treat allograft rejection, resulting in an excellent short-term and an acceptable long-term outcome. However, these drugs have potent but still non-specific immunosuppressive properties and frequently show severe acute and chronic side effects, sometimes questioning the overall success.

CONCEPTS/TRENDS:

As the "Holy-Grail" of the transplant community, the induction of "true donor-specific tolerance" has not been achieved yet; current immunosuppressive strategies, in particular in Europe, include "individually tailored immunosuppressive" protocols, mostly based on specific immunologic and non-immunologic risk factors. These protocols allow for optimal immunosuppressive protocols for each patient group according to their needs by choosing the most suitable, well-tolerated combination of agents and the most effective doses to avoid acute rejection episodes (incidence and severity) and minimise drug-related toxicity to reduce long-term drug-related morbidity and mortality. Nevertheless, transplant recipient are still being forced to take a life-long course of chemical immunosuppressive agents to keep their graft, knowing about the possible life-threatening side effects.

SUMMARY:

We review current trends of immunosuppressive protocols in liver and kidney transplantation, focusing on calcineurin-inhibitor-sparing protocols, mammalian-target-of-rapamycin (mTOR) inhibitor based-protocols and corticosteroid-avoidance protocols, being aware of the fact, that most of these strategies could be applicable for other transplanted organs, too. Finally, we describe future trends and new developments that are rising on the horizon.

10. J Ren Nutr. 2006 Oct;16(4):291-9.

Long-term evolution of body composition after renal transplantation: 5-year survey.

Moreau K[1], Chauveau P, Martin S, El-Haggan W, Barthe N, Merville P, Aparicio M.

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Acceso al artículo

Abstract

BACKGROUND:

Thanks to advancements in immunosuppression, patients are living longer with kidney transplants, and nonimmunologic factors (particularly nutritional) have become a major source of morbidity and mortality after successful kidney transplantation (KTx). In this current study, we have prospectively assessed, in a cohort of kidney transplant recipients (KTR), the course of some nonimmunologic factors liable to hinder the long-term outcome of KTR.

METHODS:

Forty-four consecutive KTR with stable functioning grafts received dietary recommendations and were on the lowest effective dose of steroids. Biochemical nutritional markers, C-reactive protein, lipid profile, and body composition determined by dual-energy X-ray absorptiometry were studied over the first year, 2 years, and 5 years after KTx.

RESULTS:

No patients died during the follow-up. All patients but 2 were considered normotensive. Clinical diabetes developed in 3 patients. Visceral proteins stabilized at a normal range after the first year. Most of the patients normalized their inflammatory status. A significant improvement in lipid profile was observed. Female patients had a significant increase of weight (13.5%), mainly because of an increase in fat mass: 3.4 kg (19.4%) at 1 year and 5.6 kg (29.7%) at 2 years. In male patients, body composition remained stable and close to baseline values. The evolution of bone mass varied according to gender, total corticoid doses, and calcineurin inhibitors. Patients on low doses of steroids normalized their Z-score over the 5-year period. The increase in bone mass (paired t-test, $P = .006$) was only significant in patients treated with tacrolimus (analysis of variance for repeated measures, $P < .001$).

CONCLUSIONS:

Simple measures and dietary intervention to prevent or correct nonimmunologic disorders should permit improvement of long-term morbidity and mortality of KTR without compromising the functional outcome of their transplant.

11. Transpl Int. 2006 Aug;19(8):629-35.

Comparison of two dosages of thymoglobulin used as a short-course for induction in kidney transplantation.

Wong W[1], Agrawal N, Pascual M, Anderson DC, Hirsch HH, Fujimoto K, Cardarelli F, Winkelmayer WC, Cosimi AB, Tolkoff-Rubin N.

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Acceso al artículo

Abstract

Thymoglobulin is used effectively as an induction agent in kidney transplantation, but the optimal dose is not well established. We evaluated the degree and durability of T-cell clearances with two different thymoglobulin regimens in adult kidney transplant recipients (KTR). Seven KTR received a 3-day thymoglobulin-based induction of 1.0 mg/kg/day while nine received 1.5 mg/kg/day, in addition to maintenance immunosuppression. Lymphocyte subsets were monitored for 6 months. Renal function, infections and malignancies were monitored for 24 months. T-cell subsets were significantly lower by day 30 with the thymoglobulin 1.5 mg/kg/day regimen when compared with the 1.0 mg/kg/day regimen; this trend was sustained at 6-month (CD3(+): 438 +/- 254 vs. 1001 +/- 532 cells/mm(3), P = 0.016). Renal function between the two groups was not significantly different at 6- and 24-months post-transplant. One case of BK Virus viremia in the 1.5 mg/kg/day thymoglobulin group was detected. No acute rejection episodes, cytomegalovirus infections, or malignancies were noted in either group. Thymoglobulin induction was efficacious in both groups, but with a significantly sustained T-cell clearance in the 1.5 mg/kg/day regimen. A more profound T-cell clearance within the first 6 months postinduction therapy may translate into a decreased risk of immunological injury and improved long-term outcome after kidney transplantation.

12. Am J Transplant. 2005 Nov;5(11):2732-9.

Effect of pregnancy on long-term kidney function in renal transplant recipients treated with cyclosporine and with azathioprine.

Fischer T[1], Neumayer HH, Fischer R, Barenbrock M, Schobel HP, Lattrell BC, Jacobs VR, Paepke S, von Steinburg SP, Schmalfeldt B, Schneider KT, Budde K.

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Acceso al artículo

Abstract

In order to investigate the effect of different immunosuppressive regimens and the time interval between transplantation and pregnancy on long-term outcome, we performed a case-control study in pregnant renal allograft recipients. Eighty-one pregnancies of kidney transplanted recipients were identified [cyclosporine (CYA): n = 40; azathioprine (AZA): n = 41]. Controls were matched with respect to important prognostic factors. Posttransplant follow-up was 91.3 +/- 5 months. Graft and patient survival were similar in both groups and there was no apparent effect of immunosuppression. A total of 28 recipients (33%) delivered within 2 years and 6 (8%) subjects within 1 year after transplantation, but these short transplantation-to-pregnancy intervals had no apparent adverse effect on long-term outcome. In contrast to AZA-treated patients, CYA-treated patients experienced an increase in serum creatinine postpartum (1.15 +/- 0.2 mg/dL vs. 1.61 +/- 0.1 mg/dL; $p < 0.05$). Whole blood CYA levels decreased transiently during pregnancy from 115.9 +/- 8 ng/mL to 80.7 +/- 7 ng/mL leading to a gradual increase in drug dose from 240 +/- 14 mg/day to 324 +/- 21 mg/day ($p < 0.05$). Following delivery, there was an increase in CYA concentrations to 173 +/- 5.4 ng/mL, requiring rapid dose tapering to baseline of 246 +/- 15 mg/day. Pregnancies in renal recipients do not affect long-term patient and graft survival, independent of the immunosuppression. No detrimental effect of short transplantation-to-pregnancy intervals on long-term graft function was detected.

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13. Transplantation. 2005 Apr 15;79(7):807-14.

Corticosteroid-free immunosuppression with tacrolimus, mycophenolate mofetil, and daclizumab induction in renal transplantation.

Rostaing L[1], Cantarovich D, Mourad G, Budde K, Rigotti P, Mariat C, Margreiter R, Capdevilla L, Lang P, Vialtel P, Ortuño-Mirete J, Charpentier B, Legendre C, Sanchez-Plumed J, Oppenheimer F, Kessler M; CARMEN Study Group.

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Acceso al artículo

Abstract

BACKGROUND:

Corticosteroid-free maintenance immunosuppression after organ transplantation eliminates the well-known corticosteroid-related side effects and may help to improve long-term outcome. We investigated whether a corticosteroid-free tacrolimus (Tac)/mycophenolate mofetil (MMF) regimen, in combination with daclizumab (Dac) induction therapy, provides adequate immunosuppression after renal transplantation.

METHODS:

This 6-month, open-label, multicenter, parallel-group study involved 538 renal patients randomized (1:1) to a Dac/Tac/MMF regimen (n = 260) or a Tac/MMF/corticosteroids regimen (n = 278) as a control group.

RESULTS:

Of the patients who completed the study, 88.8% in the Dac/Tac/MMF group were free from corticosteroid therapy at month 6. The incidence of biopsy-proven acute rejection was 16.5% in both treatment groups; the incidence of biopsy-proven corticosteroid-resistant acute rejection was 4.3% and 5.0% with Tac/MMF/corticosteroids and Dac/Tac/MMF, respectively (P = NS for both comparisons). Renal function was also similar in both groups: median serum creatinine at month 6 was 125.0 micromol/L (Tac/MMF/corticosteroids) and 131.0 microml/L (Dac/Tac/MMF), P = 0.277. The overall safety profile was similar with both regimens. However, compared with the Tac/MMF/steroid regimen, a significantly reduced incidence of new-onset insulin-dependent diabetes mellitus (5.4% vs. 0.4%, P = 0.003) was found with steroid-free immunosuppression. Moreover, mean total cholesterol concentrations increased from baseline in the Tac/MMF/corticosteroids group by 0.19 mmol/L, whereas in the Dac/Tac/MMF group, levels decreased by 0.19 mmol/L, P = 0.005.

CONCLUSIONS:

Corticosteroid-free immunosuppression with a Dac/Tac/MMF regimen is as effective at preventing acute rejection after renal transplantation as a standard triple regimen of Tac/MMF/corticosteroids. Furthermore, the safety benefits reported with Dac/Tac/MMF treatment may help improve the long-term outcome for renal-transplant patients.

14. Clin Transplant. 2005 Apr;19(2):153-7.

The long-term outcome of tacrolimus in cadaveric kidney transplantation from non-heart beating donors.

Fukuhara N[1], Ono Y, Hattori R, Nishiyama N, Yamada S, Kamihira O, Kinukawa T, Ohshima S.

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Acceso al artículo

Abstract

Tacrolimus (Tac), developed in 1990, has been applied as an immunosuppressive agent for liver, heart, and kidney transplantation and is known to have more powerful immunosuppressive effects than cyclosporine (CyA). To evaluate the efficacy of Tac in cadaveric kidney transplants from non-heart beating donors, we present the long-term outcome of patients receiving kidneys with ischemic damage, and compared it with that of CyA. Between July 1990 and December 2000, 55 patients with end-stage renal disease received kidneys from non-heart beating donors (Maastrichy category 3) and were treated with Tac and steroid immunosuppressive therapy. During the same period, we also performed 137 non-heart beating cadaveric renal transplants treated with CyA-based immunosuppressive therapy. The patient survival rate was 98% at 1 yr and 96% at 3-10 yr in the Tac group, and 97% at 1-3 yr, 93% at 5 yr and 85% at 10 yr in the CyA group. The graft survival rate was 91% at 1 yr, 80% at 3 yr, 63% at 5 yr and 34% at 10 yr in the Tac group, and 88% at 1 yr, 75% at 3 yr, 63% at 5 yr and 49% at 10 yr in the CyA group. There was no significant difference in either patient or graft survival rates between the two groups. Acute early rejection in the Tac group was less than that in the CyA group but acute tubular necrosis was the same in both groups. This indicates that Tac is available for cadaveric kidney transplants from non-heart beating donors. In conclusion, Tac is available as an immunosuppressive agent even for kidney transplants from non-heart beating donors.

15. Transplant Proc. 2004 Sep;36(7):2105-7.

Evaluation of cyclosporine C2 levels in long-term stable renal allograft recipients.

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Acceso al artículo

Abstract

BACKGROUND:

The use of cyclosporine was traditionally monitored by the trough level (C(0)). However, the immunosuppressive effects of cyclosporine correlate with its drug exposure, represented by the area under curve (AUC). It was also noted that cyclosporine C(0) level correlated with AUC poorly, while C(2) level (concentration at 2 hours after drug administration) satisfactorily correlated with AUC. Most recent studies concern the use of C(2) levels in de novo renal transplant patients; target levels of C(2) have been suggested. There is rare discussion about the C(2) target level for long-term cyclosporine-maintenance patients. Our objectives were to analyze the cyclosporine C(2) levels of patients more than 12 months after transplantation as well as changes in C(2) with time and the correlation between C(2) level and renal function.

METHODS AND PATIENTS:

This was a cross-sectional case-controlled study of 101 kidney recipients immunosuppressed with a cyclosporine-based regimen for at least 12 months. Both C(0) and C(2) levels were examined at various time points during outpatient clinic follow-up. The patients were stratified according to the time after transplant surgery, or to their renal function.

RESULTS:

The 101 patients were divided into three groups based on the time after renal transplant surgery. Groups 1, 2, and 3 represented patients transplanted for 1 to 3 years (n = 16), 4 to 6 years (n = 35), and more than 6 years (n = 50), respectively. The C(2) levels for each group were 657 +/- 232, 561 +/- 186, and 580 +/- 243 ng/mL, respectively, (P = NS). When stratified into low versus high C(2) groups, there were no significant differences in renal function both at the beginning and at the end of 1 year follow-up. Seven of 67 patients shifted to stronger immunosuppression in the low C(2) group, but only 2/34 in the high C(2) group, a difference that was not significant (P = .234 by Fisher Exact Test). Patients with creatinine levels greater than 1.5 mg/dL or lower than 1.5 mg/dL showed no difference in C(2) on C(0) levels. Patients with deterioration of renal function during this period had no different C(2) levels as those with no deterioration of renal function.

CONCLUSION:

The average C(2) levels among long-term cyclosporine-maintained patients were significantly lower than those previously suggested. C(2) levels did not correlate with the long-term outcome of renal function in patients at least 1 year after renal transplantation.

16. Clin Transplant. 2003 Dec;17(6):518-21.

Long-term outcome of kidney transplant using non-heart-beating donor: multicenter analysis of factors affecting graft survival.

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Acceso al artículo

Abstract

This multicenter study was retrospectively evaluated for the predictive factors affecting the long-term graft survival of a kidney transplant from a non-heart-beating donor (NHBD).

PATIENTS AND METHOD:

A total of 706 patients received transplants from NHBD in 11 centers between 1986 and 2000 and the results were entered into the analysis. The patients were treated with cyclosporine- or tacrolimus-based immunosuppressive therapy. Graft survival was calculated by the Kaplan-Meier method. Factors selected for univariate analysis were donor age, and acute early and acute late rejection. Hypertension (HT), hyperlipidemia (HL), and diabetes mellitus were also analyzed in 638 recipients whose graft survived for more than 1 yr.

RESULTS:

In the cases using NHBD, graft survival for 1, 5, and 10 yr was 87, 69, and 53%, respectively. Donor age of over 55 yr, acute early and late rejection, post-transplant HT and diabetes at the first post-operative year were shown to be significantly harmful on long-term graft survival. For longer graft survival in NHBD kidney transplantations, reducing acute rejection, and controlling blood pressure and sugar are crucial.

17. Kidney Int. 2003 Aug;64(2):674-80.

Ten-year survival of second kidney transplants: impact of immunologic factors and renal function at 12 months.

Coupel S[1], Giral-Classe M, Karam G, Morcet JF, Dantal J, Cantarovich D, Blancho G, Bignon JD, Daguin P, Soulillou JP, Hourmant M.

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Acceso al artículo

Abstract

BACKGROUND:

The aim of the present study was to assess long-term survival of cadaveric second kidney allografts performed in our center and to determine risk factors predictive of long-term graft outcome.

METHODS:

Of 1704 kidney transplantations performed between January 1985 and March 1998, 233 were second grafts. The majority of the recipients were sensitized. All patients were treated with the same quadruple immunosuppressive regimen.

RESULTS:

Kaplan-Meier analysis documented graft survival of 89% at 1 year, 76% at 5 years, and 53% at 10 years. Graft survival was similar for second and primary kidney transplants performed during the same period of time. When long-term second graft survival was examined, only two risk factors were found to be significant: (1) the degree of human leukocyte antigen (HLA) DR mismatch (MM) and (2) the number of acute rejection episodes. Multivariate analysis of several pre- and posttransplant variables also confirmed the importance of HLA MM (DR> A), but also, identified serum creatinine at 12 months as the most significant predictor of graft survival. In addition, the Cox proportional hazards model revealed that only the year of transplantation had an independent significant effect on acute rejection occurrence (RR = 0.591, 95%CI 0.437 to 0.801, P < 0.0007). Indeed, the incidence of acute rejection was found to decrease over time (44% of patients experienced at least one episode of acute rejection before 1990 vs. 17% after 1990).

CONCLUSION:

Finally, second graft long-term outcome shows an improved evolution according to the time period resulting from a strong decrease in acute rejection incidence and the impact of creatinine at 12 months.

19. Nephrol Dial Transplant. 2003 May;18 Suppl 1:i3-6.

Renal function as a predictor of long-term graft survival in renal transplant patients.

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Acceso al artículo

Abstract

Acute rejection is a major risk factor for kidney graft failure. However, as acute rejection has been progressively reduced by recent immunosuppressive regimens, other risk factors are becoming increasingly important. Evidence is accumulating that early renal function predicts long-term outcome. A recent registry survey of more than 100 000 kidney transplants found that 6- and 12-month serum creatinine levels, as well as the change between 6 and 12 months, are strongly associated with long-term graft survival. A survey of paediatric renal transplant recipients showed that poor creatinine clearance (<50 ml/min) as early as 30 days post-transplant predicted an annual rate of graft loss of 13% compared with <3% in patients with 30-day clearance >50 ml/min. This association between early renal function and long-term outcome was confirmed in multicentre studies. Renal transplant recipients (n=572) with 6-month serum creatinine levels >1.5 mg/dl suffered 3-year graft loss of 19.3% compared with only 8.5% in patients with levels <1.6 mg/dl (P<0.001). Significantly fewer patients receiving tacrolimus had 12-month serum creatinine levels >1.5 mg/dl compared with cyclosporin (42 versus 54%, P<0.05). Interestingly, a single-centre study (n=436) found that while glomerular filtration rate (GFR) at 6 months post-transplant had remained stable over the last decade, the rate of loss of renal function had decreased. A lower rate of GFR loss was associated with absence of rejection, use of mycophenolate mofetil rather than azathioprine and use of tacrolimus rather than cyclosporin (P<0.01). In conclusion, early measures of renal function allow identification of those patients at highest risk of graft failure and provide an invaluable tool for improving outcomes by tailored immunosuppression. The choice of such immunosuppression should be guided not only by its ability to prevent rejection, but also by its impact on renal function.

Free Article

20. Transplant Proc. 2003 May;35(3 Suppl):67S-72S.
Optimizing the long-term outcome of renal transplants: opportunities created by sirolimus.
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Acceso al artículo

Abstract
This review focuses upon the sirolimus-based cyclosporine elimination studies and the light they shed on choice of the best long-term immunosuppressive strategy for managing the balance between prevention of loss of grafts from antigen specific immune responses or from chronic nephrotoxicity. The underlying strategy of both cyclosporine elimination studies was to treat patients with a uniform therapy for the first 3 months and then wean off the cyclosporine therapy in one cohort. The Phase II study was conducted in 246 recipients in 17 centers in the USA and Europe. Thus 97 patients were treated with full-dose cyclosporine, fixed-dose sirolimus and corticosteroids, and 100 patients received reduced-dose cyclosporine and trough concentration controlled sirolimus with corticosteroids until 3 months when the dose of cyclosporine was tapered progressively. The phase III study was undertaken in 525 patients in 57 centers in Australia, Canada and Europe with randomization for cyclosporine elimination undertaken at 3 months and implemented over the next 4-6 weeks. The primary outcome of renal function was better in the elimination arms of both studies and, in the phase III study, continued to improve for up to 2 years. Both studies demonstrated better renal function, equivalent patient and graft survival and no difference in acute rejection rates. These studies have shown that one of the successful strategies for improving the longer term graft survival rates includes the continuous use of sirolimus and steroids, without calcineurin inhibitors.

21. Transplant Proc. 2002 Aug;34(5):1577-9.
Long-term outcome of tacrolimus in cadaveric kidney transplantation from non-heart-beating donors.
Fukuhara N[1], Ono Y, Kinukawa T, Hattori R, Nishiyama N, Yamada S, Kamihira O, Ohshima S.

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Acceso al artículo

22. Hepatogastroenterology. 2001 Jan-Feb;48(37):169-73.

Long-term outcome of kidney transplantation in patients with hepatitis C virus infection.

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Abstract

BACKGROUND/AIMS:

The impact of HCV (hepatitis C virus) infection on the long-term outcome of kidney transplant patients is controversial.

METHODOLOGY:

Eighty-four renal allograft recipients who were seronegative for hepatitis B surface antigen and had been screened for antibody to hepatitis C virus (anti-HCV) were included. The outcome and survival were compared between anti-HCV-positive (n = 30, group 1) and anti-HCV-negative (n = 54, group 2) kidney transplant patients. Group 1 patients were further compared to 52 anti-HCV-positive end-stage renal disease patients (group 3) who were on chronic dialysis.

RESULTS:

Group 1 patients had a higher prevalence of chronic hepatitis than group 2 and group 3 patients did (67% vs. 2% and 31%). Liver-related complications and deaths between group 1 and group 2, and group 1 and group 3 patients were not significantly different. The comparisons of the long-term survival between these groups showed no significant differences, despite group 3 patients had a higher overall mortality rate. Cox regression analysis confirmed that age more than 45 years was the only independent factor that affected survival in anti-HCV-positive end-stage renal disease patients with or without kidney transplantation.

CONCLUSIONS:

HCV infection is not a contraindication to kidney transplantation. For anti-HCV-positive end stage renal disease patients, survival is better in younger patients, and is not influenced by kidney transplantation or continuing dialysis.

23. Surg Today. 2001;31(6):492-6.

Long-term outcomes of immunosuppressed renal transplant recipients with malignancies.

Gunji Y[1], Sakamoto K, Kamura K, Yamada K, Kashiwabara H, Shimada H, Hori S, Suzuki T, Ochiai T.

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Acceso al artículo

Abstract

This study analyzes ten cases of malignancy in a cohort of 183 renal transplant recipients, examining surgical management, postoperative immunosuppressive therapy, and long-term outcome. One of these ten patients, who had malignant lymphoma of the jejunum, died of the neoplasm, but the other nine patients did not show any signs of tumor recurrence after removal. All of these nine patients, except for one who had transplant renal cell carcinoma (RCC), received the same dose of immunosuppressive agents after surgery for the malignant disease. Seven patients were still alive at the time of this report, six of whom had good transplant renal function. The findings of this study indicate that even if immunosuppressive agents predispose to the development of cancer, it is not necessary to reduce their dose after removal of the tumor.

24. Am J Transplant. 2005 Jul;5(7):1748-56.

Calcineurin inhibitor withdrawal from sirolimus-based therapy in kidney transplantation: a systematic review of randomized trials.

Mulay AV[1], Hussain N, Fergusson D, Knoll GA.

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Abstract

Calcineurin inhibitor (CNI) withdrawal has been used as a strategy to improve renal allograft function, however, it also carries risk of acute rejection. We conducted a systematic review of randomized trials that involved CNI withdrawal from a sirolimus-based immunosuppressive regimen. The search strategy yielded six trials (n = 1047 patients) reported in eight publications. CNI withdrawal from sirolimus-based therapy, was associated with an increased risk of acute rejection (risk difference, 6%; 95% CI 2-10%, p = 0.002) but a higher creatinine clearance (mean difference, 7.49 mL/min; 95% CI 5.08-9.89 mL/min, p < 0.00001) at 1 year compared to continued CNI and sirolimus therapy. Graft loss (relative risk, 0.87; 95% CI 0.46-1.64, p = 0.66) and death (relative risk, 0.88; CI 0.40-1.96, p = 0.76) were similar in both groups at 1 year. Hypertension was significantly reduced in the CNI withdrawal group (relative risk, 0.56; 95% CI 0.40-0.78, p = 0.0006). CNI withdrawal from sirolimus-based therapy is associated with an increased risk of acute rejection in the short term with a significant improvement in renal function and a reduction in hypertension. Longer follow-up is needed to determine if these changes will result in a significant improvement in patient and graft survival.

25. Transplantation. 2010 Apr 27;89(8):962-7.

Beyond histology: lowering human leukocyte antigen antibody to improve renal allograft survival in acute rejection.

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Abstract

BACKGROUND:

The common endpoint in the treatment of antibody-mediated rejection (AMR) is functional reversal (creatinine levels). Reduction of human leukocyte antigen (HLA) antibody strength is not commonly considered as an essential endpoint for AMR resolution. The purpose of this study was to determine whether reduction in HLA antibody intensity in patients with histologic AMR reversal influences long-term renal allograft survival.

METHODS:

Renal allograft recipients were included if he or she had a biopsy diagnosis of AMR (between August 2000 and October 2008) and serial evaluation for HLA antibodies prebiopsy and postbiopsy. Antibody reduction was defined as mean fluorescence intensity decrease more than 50% in highest intensity antibody after AMR therapy and the absence of new antibody formation. Patients were treated with plasmapheresis, thymoglobulin/OKT3, and corticosteroids. Survival analysis was performed using STATA/MP v10 (College Station, TX).

RESULTS:

Twenty-eight patients were analyzed. Antibody reduction failed to occur in 22 of 28 cases. Baseline characteristics were similar between groups. Antibody nonresponders had significantly shorter allograft survival time (61.4 months) compared with antibody responders (no failures) (P=0.04, log-rank test).

CONCLUSIONS:

In conclusion, failure to significantly reduce antibody levels and prevent new formation was strongly predictive of allograft loss. This observation suggests that the therapeutic intervention that reduces antibody production may prolong graft survival in transplantation.

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