Clinical outcomes of 11,436 kidney transplants performed in a single center - Hospital do Rim

Desfechos clínicos de 11.436 transplantes renais realizados em centro único – Hospital do Rim

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Abstract

Introduction: Kidney transplantation is considered a cost-effective treatment compared to dialysis but accounts for a significant percentage of the public health care resources. Therefore, efficient systems capable of performing high number of procedures are attractive and sustainable. **Objective:** The aim of this study was to evaluate clinical outcomes of 11,436 kidney transplants regularly performed in a single transplant dedicated center over the last 18 years. **Methods:** This was a retrospective study performed in a single specialized transplant center. All consecutive patients who underwent transplantation between 08/18/1998 and 12/31/2015 were included in the analysis. **Results:** The annual number of transplants increased from 394 in 1999 to 886 in 2015, with a progressive reduction in the proportion of living donor kidney transplants (70% *vs.* 23%) and yielding over 8869 patients in regular follow up. Of 11,707 kidney transplants performed, 5348 (45.7%) were from living, 3614 (30.9%) standard and 1618 (13.8%) expanded criteria deceased donors, 856 (7.3%) pediatric and 271 (2.3%) simultaneous kidney-pancreas transplants. Comparing 1998-2002 and 2011-2014, five-years graft survival increased for kidney transplants performed with living donors (83.3% *vs.* 93.1%, $p < 0.001$), standard deceased donors (60.7% *vs.* 79.7%, $p < 0.001$), expanded criteria donors (46.5% *vs.* 71.5%, $p < 0.001$) and for the pediatric population (79.8% *vs.* 80.9%, $p = 0.684$). **Conclusion:** The implementation of a dynamic and efficacious health care system was associated with a progressive increase in the number of kidney transplants, in the cumulative number of patients in follow up and a shift from living related to deceased donor kidney transplants, with associated progressive increase in patient and graft survivals.

Keywords: kidney transplantation; outcome assessment (health care); health information management; immunosuppression.

Resumo

Introdução: Transplante renal é considerado um tratamento custo-efetivo comparado à diálise e representa uma porcentagem significativa dos recursos de saúde pública. Dessa forma, sistemas eficientes e capazes de realizar um elevado número de procedimentos, são atraentes e sustentáveis. **Objetivo:** O objetivo deste estudo foi avaliar os desfechos clínicos de 11.436 transplantes renais realizados em um centro único de transplante nos últimos 18 anos. **Métodos:** Trata-se de um estudo retrospectivo realizado em centro único e especializado em transplante renal. Todos os pacientes transplantados entre 18/08/1998 e 31/12/2015 foram incluídos nesta análise. **Resultados:** O número anual de transplantes aumentou de 394 em 1999 para 886 em 2015, com redução progressiva na proporção de transplantes realizados com doador vivo resultando em mais de 8869 pacientes em seguimento regular. De 11.707 transplantes renais realizados, 5348 (45,7%) foram de doador vivo, 3614 (30,9%) doador falecido padrão e 1618 (13,8%) de critério expandido, 856 (7,3%) pediátricos e 271 (2.3%) transplantes simultâneo rim-pâncreas. Comparando 1998-2002 e 2011-2014, a sobrevida do enxerto em 5 anos aumentou para os transplantes renais realizados com doador vivo (83,3% *vs.* 93,1%, $p < 0,001$), doador falecido padrão (60,7% *vs.* 79,7%, $p < 0,001$), falecido de critério expandido (46,5% *vs.* 71,5%, $p < 0,001$) e para a população pediátrica (79,8% vs. 80,9%, $p = 0,684$). **Conclusão:** A implementação de um sistema de saúde eficaz e dinâmico associou-se ao aumento progressivo no número de transplantes renais, no número cumulativo de pacientes em acompanhamento e na inversão do número de transplantes realizados com doador vivo para falecido. Houve um aumento progressivo na sobrevida do enxerto e do paciente, reforçando que este modelo pode ser aplicado em outras áreas terapêuticas.

Palavras-chave: transplante de rim; avaliação de resultados (cuidados de saúde); gestão da informação em saúde; imunossupreção.

Introduction

Brazil has developed successful models of public funded, high complexity and high-cost health assistance that is beyond the expectations of a developing country. The Brazilian health system is composed of a large public, government managed system (Sistema Único de Saúde, SUS), which serves the majority of the population, and a private sector, managed by health insurance funds and private entrepreneurs.[1]

The national transplant program is surpassed only by the United States in absolute numbers. Within the national transplant system each of the 27 Brazilian States has one Notification, Donation and Procurement Central Office (CNCDO), located at the State Health Secretariat, which coordinates one or more organ procurement organizations (OPOs), depending on the size of the state population.[2] This adequately organized and funded program allowed the establishment and growth of many transplant centers throughout the country.

Hospital do Rim (Hrim) is one of these transplant centers that was inaugurated in the end of 1998 with the intention to develop a unique medical care model, aiming to perform at least one kidney transplant per day. The progressive development and perfectioning of this model resulted in steady growth of the annual number of transplants over this 18-year period, reaching over 850 kidney transplants performed every year since 2009.[3] Currently, patients from all regions of the country are referred to Hrim for transplantation and more than 90% of the procedures are financed by SUS.[4]

Kidney transplantation is a complex therapeutic area where high volume and progressive increase in complications accumulates over time, challenging clinical management even in highly organized medical care systems. Here we provide robust data showing that this unique health care model, not only allows increasing the number of transplants over time, but is also associated with progressive improvement in survival outcomes as well as the quality of care.

Methods

Study design

This is a retrospective study performed in a single transplant center. The data was obtained by searching electronic database provided by the Collaborative Transplant Study (Heidelberg, Germany).[5] Follow up data were collected until July 2016. The study was approved by the local Research Ethics Committee (CEP) at UNIFESP under registration C.A.A.E ID: 57254216.0.0000.5505.

Study population and objectives

For this analysis, all consecutive recipients of kidney or kidney/pancreas transplantation between 08/18/1998 and 12/31/2015 were included. Simultaneous kidney-pancreas transplantations are not considered an individual group for analysis. We described demographic characteristics, immunosuppression, incidence of acute rejection, graft loss, death, and renal function. Also, time-dependent changes for each of these parameters were compared, stratified by donor type.

Definitions

Delayed graft function was defined as the need for dialysis during the first week after transplantation. Expanded criteria donors were those aged over 60 years old or those between 50 and 59 years old who presented at least two of the following criteria: hypertension, cerebrovascular death and final serum creatinine above 1.5 mg/dL. All treated acute rejection episodes were included in the analysis, including those confirmed or not by histopathological evaluation. Graft loss was defined as the need for permanent return to dialysis. Loss to follow-up was defined by the lack of information for more than 6 consecutive months.

Statistical analysis

Continuous variables were presented by mean and standard deviation and categorical variables were presented as frequency and percentage. The differences between groups were identified using the Student t test or Chi square test, respectively. The differences in cumulative survival obtained by the Kaplan-Meier curves were identified by Log Rank test.

To analyze changes in demographic characteristics and immunosuppression we compared data from 1998-2000 with 2015. To analyze changes in renal function we compared data from 1998-2000 with 2013-2014. Two cohorts of patients (1998-2000 and 2013-2014) were used to compare time dependent changes in selected key efficacy outcomes.

Because the first simultaneous kidney/pancreas transplant was performed in 2002, the two cohorts of

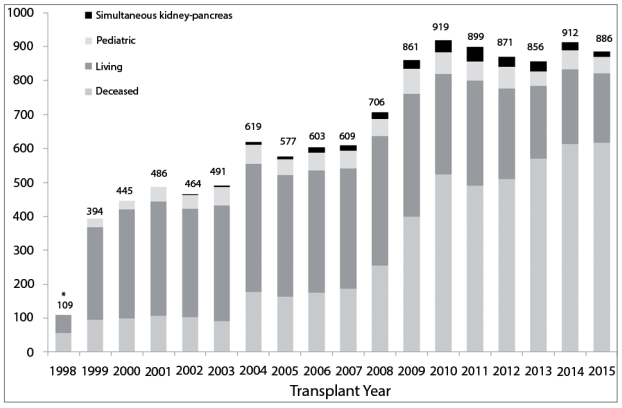
patients used to compare time dependent changes in selected key outcomes were 2002-2005 and 2014. All statistical analyzes were performed using SPSS version 18 (SPSS Inc., Chicago, IL, USA) and differences were considered significant for values of $p < 0.05$.

Results

Annual number of transplants

From August 18th, 1998 to December 31th, 2015 11,436 kidney transplants were performed, 5348 (45.7%) living donor kidney transplants, 3614 (30.9%) standard deceased donors transplant, 1618 (13.8%) expanded criteria donor transplants, 856 (7.3%) pediatric kidney transplants and 271 (2.3%) simultaneous kidney-pancreas transplants were performed (Figure 1). From 1998 to 2009 there was a progressive increase in the number of transplants, primarily due to increase deceased donation. As a consequence, the proportion of living donor kidney transplants was reduced from 70% in 1998-2000 to 23% in 2015.

Figure 1. Annual number of kidney transplants performed at Hrim from 1998 to 2015, according to transplant origin. * Number of transplants from August to December, 1998.



Demographic characteristics

The demographic characteristics of the transplant population are shown in Table 1. There were 5348 living donor kidney transplants. From 1998-2000 (n = 643) to 2015 (n = 205) there were no differences in recipient age (38.1 ± 11.1 *vs.* 37.8 ± 11.7 years, $p = 0.702$) and time on dialysis (23.5 ± 20.9 *vs.* 21.3 ± 24.6 months, $p = 0.227$) but donor age increased significantly (42.5 ± 11.8 and 45.3 ± 10.4 years, $p = 0.002$).

Of 5232 deceased donor kidney transplants, 3614 (69%) were from standard and 1618 (31%) from expanded criteria donors. From 1998-2000 to 2015 the number of deceased donor kidney transplants increased from 253 (224 standard, 29 expanded) to 617 (418 standard, 199 expanded).

Among standard deceased donor kidney transplants from 1998-2000 to 2015, donor age (31.7 ± 12.8 *vs.* 39.6 ± 11.4 years, $p < 0.001$), as well as, recipient age (42.3 ± 10.9 *vs.* 46.7 ± 12.9 years, $p < 0.001$), and cold ischemia time (20.4 ± 8.3 *vs.* 23.8 ± 6.6 hours, $p < 0.001$), respectively, increased but the proportion of retransplants decreased (16.1% *vs.* 10.5%, $p = 0.043$).

Likewise, among expanded deceased donor kidney transplants from 1998-2000 to 2015, the donor age (56.6 ± 3.9 *vs.* 60.3 ± 6.5 years, $p < 0.001$), recipient age (41.5 ± 11.8 *vs.* 50.3 ± 11.4 years, $p < 0.001$), and cold ischemia time (20 ± 8.5 *vs.* 23.5 ± 6.2 hours, $p < 0.039$) increased, but time on dialysis (84.9 ± 37.5 *vs.* 49.9 ± 39.3 months, $p < 0.001$) and retransplants (13.8% *vs.* 4%, $p = 0.028$) decreased over time.

Among 856 pediatric transplants, 238 (28%) were from living and 618 (72%) from deceased donors. There were no significant differences in the annual number of pediatric kidney transplants, ranging from 24 to 74 per year, but the proportion of living donors decreased from 1998-2000 to 2015 (71.2% to 8.3%, $p < 0.001$), respectively. Living donor age (40.9 ± 9.2 and 43.0 ± 8.2 years, $p = 0.638$) were no different but deceased donor age (18.3 ± 15.8 and 11.3 ± 6.5 years, $p < 0.001$) and time on dialysis (22.4 ± 19.6 *vs.* 13.5 ± 11.8 months, $p = 0.013$) decreased while cold ischemia time among deceased donors (9.8 ± 5.4 and 23.9 ± 6.8 hours, $p < 0.039$) increased comparing cohort of 1998-2000 and 2015.

After the first simultaneous kidney/pancreas transplant in 2002 an increase in the annual number up to 42 transplants in 2011 was observed, with subsequent decrease to about 16 transplants per year. While no changes in donor age (25.8 ± 10.2 *vs.* 23.1 ± 5.3 years), recipient age (38.5 ± 7.8 *vs.* 37.1 ± 7.6 years) and kidney delayed graft function (14.3% *vs.* 25%) were observed, patients transplanted in 2015 had longer time on dialysis (34.7 ± 45.3 *vs.* 59.8 ± 20.4 months, $p = 0.047$) comparing to 2002-2005. Also, a significant decrease in kidney (18 ± 15 *vs.* 10 ± 3, hours, $p = 0.045$) and pancreas (14.8 ± 4.8 *vs.* 9.5 ± 3.1 hours, $p = 0.045$) cold ischemia times was observed.

Immunosuppression

Overall, induction therapy was used in 14.1% of recipients of living donor kidneys, in 53.3% of recipients of standard deceased, 82.6% in recipients of expanded deceased and 76.2% in pediatric recipients. The use of induction therapy increased

Table 1 Demographic characteristics of the transplant population according to transplant origin

Variable	Living Donors (N = 5348)	Deceased Standard (N = 3614)	Deceased Expanded (N = 1618)	Pediatrics Transplants (N = 856)
Recipient age, years (mean ± SD)	38.8 ± 11.5	46.2 ± 12.8	49.6 ± 11.8	12.2 ± 4.1
Recipient gender, male, N (%)	3358 (63%)	2120 (59%)	993 (61%)	482 (56%)
Recipient ethnicity, N (%)				
White	3457 (64.6%)	1906 (52.7%)	808 (49.9%)	519 (60.6%)
Black	1086 (20.3%)	840 (23.3%)	353 (21.8%)	154 (18%)
Miscegenated	640 (12%)	614 (17%)	315 (19.5%)	153 (17.9%)
Other	165 (3.1%)	254 (7%)	142 (8.8%)	30 (3.5%)
Cause of chronic kidney disease, N (%)				
Glomerulonephritis	1387 (25.9%)	657 (18.2%)	274 (16.9%)	245 (28.6%)
Hypertension	82 (1.5%)	146 (4.0%)	60 (3.7%)	0 (0.0)
Nephroesclerosis	289 (5.4%)	369 (10.2%)	171 (10.6%)	4 (0.5%)
Diabetes Mellitus	355 (6.6%)	494 (13.7%)	266 (16.4%)	1 (0.1%)
Polycystic Kidney Disease	354 (6.6%)	292 (8.1%)	154 (9.5%)	28 (3.3%)
Undetermined	2207 (41.3%)	1216 (33.6%)	543 (33.6%)	267 (31.2%)
Other	674 (12.6%)	440 (12.2%)	150 (9.3%)	311 (36.3%)
Time on dialysis, months (mean ± SD)	23.7 ± 26.9	59.8 ± 47.2	55.5 ± 43.5	21.3 ± 21.2
Type of treatment, N (%)				
Hemodialysis	4362 (81.6%)	3254 (90.1%)	1458 (90.2%)	508 (59.3%)
Peritoneal dialysis	289 (5.4%)	167 (4.6%)	89 (5.5%)	212 (24.8%)
Conservative	629 (11.8%)	28 (0.8%)	13 (0.8%)	75 (8.8%)
Hemodialysis and Peritoneal	66 (1.2%)	163 (4.5%)	57 (3.5%)	61 (7.1%)
Panel reactive antibodies, (%)				
class I (mean ± SD)	4.5 ± 15.4	10.6 ± 23.5	7.3 ± 18.9	4.9 ± 15.7
class II (mean ± SD)	3.7 ± 14.5	6.3 ± 18.9	5.3 ± 17.5	2.1 ± 11.1
Diabetes status, N (%)	247 (8.1)	438 (15.5)	251 (17.6)	5 (0.9)
CMV IgG serologic status, N (%)				
Donor(+)/Recipient(+)	2795 (72.7)	1132 (43)	600 (44.3)	235 (39.3)
Donor(+)/Recipient(-)	245 (6.4)	122 (4.6)	59 (4.4)	66 (11.0)
Donor(-)/Recipient(+)	124 (3.2)	276 (10.5)	178 (13.1)	65 (10.9)
Donor(unk)/Recipient(+)	573 (14.9)	1000 (38.0)	464 (34.2)	195 (32.6)
Donor(-)/Recipient(-)	56 (1.5)	22 (0.8)	14 (1.0)	9 (1.5)
Donor(unk)/Recipient(-)	49 (1.3)	80 (3.1)	41 (3.0)	28 (4.7)
Donor age, years (mean ± SD)	44.3±10.7	37.8±11.9	59.3 ± 6.5	20.6 ± 14.9
Donor gender, male, N (%)	2191 (41%)	2219 (61.4%)	825 (51%)	490 (57.2%)
Donor ethnicity, N (%)				
White	3123 (66.4%)	1830 (60.2%)	849 (60.3%)	473 (67%)
Black	843 (17.9%)	476 (15.7%)	204 (14.5%)	96 (13.6%)
Miscegenated	654 (13.9%)	677 (22.3%)	323 (22.9%)	130 (18.4%)
Other	83 (1.8%)	55 (1.8%)	32 (2.3%)	7 (1.0%)
Cold ischemia time, hours (mean ± SD)	Not applicable	23.1 ± 6.6	23.9 ± 6.2	22.1 ± 6.1

from 1998-2000 to 2015 in all types of transplants (living donor: 2% to 83% [79% r-ATG, 4% anti-IL2R]; standard deceased: 4% to 99% [96% r-ATG, 3% anti-IL2R]; expanded deceased: 7% to 100% [100% r-ATG]; and pediatric recipients: 11.5% to 96% [8% r-ATG, 88% anti-IL2R]) (Table 2).

Table 2 Initial immunosuppression of the transplant recipients according to transplant origin

	Living Donors (N = 5348)	Deceased Standard (N = 3614)	Deceased Expanded (N = 1618)	Pediatrics Transplants (N = 856)
Induction therapy, n (%)				
rATG	293 (5.5%)	1244 (34.4%)	1055 (65.2%)	40 (4.7%)
Anti IL2R	460 (8.6%)	684 (18.9%)	281 (17.4%)	612 (71.5%)
None	4596 (85.9%)	1686 (46.7%)	282 (17.4%)	204 (23.8%)
Initial immunosuppression, n (%)				
TAC+Pred+AZA	1982 (37.1%)	1603 (44.4%)	231 (14.3%)	590 (68.9%)
TAC+Pred+MPA	681 (12.7%)	1295 (35.8%)	1096 (67.7%)	88 (10.3%)
CsA+Pred+AZA	1550 (29.0%)	203 (5.6%)	26 (1.6%)	133 (15.5%)
CsA+Pred+MPA	298 (5.6%)	147 (4.1%)	36 (2.2%)	31 (3.6%)
TAC+Pred+EVR	112 (2.1%)	162 (4.5%)	92 (5.7%)	0 (0.0)
CsA+Pred+EVR	120 (2.3%)	8 (0.2%)	0 (0.0)	0 (0.0)
TAC+Pred+SRL	121 (2.3%)	20 (0.5%)	5 (0.3%)	1 (0.1%)
CsA+Pred+SRL	224 (4.2%)	15 (0.4%)	1 (0.1%)	4 (0.5%)
Others	260 (4.9%)	161 (4.5%)	131 (8.1%)	9 (1.1%)

Anti IL2R: anti-interleukin-2 receptor; AZA: Azathioprine; CsA: Cyclosporine; EVR: Everolimus; MPA: Mycophenolic acid; Pred: Prednisone; rATG: rabbit antithymocyte globulin; SRL: Sirolimus; TAC: Tacrolimus.

Over time, there was a gradual replacement of cyclosporine by tacrolimus and azathioprine by mycophenolate. While the use of cyclosporine, combined with azathioprine and prednisone, was predominant in 1998-2000 (72% of living and 86% of standard deceased donor kidney transplant), the use of tacrolimus increased over time reaching 65% of living and 92% of standard deceased donors in 2015, always associated with azathioprine (56%) or mycophenolate (36%).

Whereas 93.1% of recipients of expanded criteria deceased kidneys were receiving cyclosporine, prednisone, azathioprine in 1998-2000, 84% were receiving tacrolimus, prednisone, mycophenolate acid in 2015. Similarly, 88.5% of pediatric kidney transplant recipients received cyclosporine, azathioprine and prednisone in 1998-2000 while 83.3% received tacrolimus, azathioprine and prednisone in 2015. Finally, more than 92% of kidney-pancreas transplant recipients received tacrolimus, mycophenolate and prednisone from 2002 to 2015.

Efficacy

Among recipients of living donor kidney transplants, the overall incidence of first treated acute rejection, death, and graft loss during the first year were 23.8%, 2.1%, and 2%, respectively. Comparing 1998-2000 to 2013-2014 a decrease in the incidence of death and graft loss was observed during the first year after transplantation (Table 3).

Among recipients of standard deceased donor kidney transplants, the overall incidence of first treated acute rejection, death, and graft loss were 26.5%, 6.8%, and 6%, respectively. Corresponding figures for expanded deceased donor kidney transplants were 23.2%, 8.2%, and 8.5%, respectively. Comparing 1998-2000 to 2013-2014 a decrease in the incidence of treated rejection, death and graft loss was observed during the first year after transplantation for recipients of standard and expanded deceased donor kidney transplants. In the pediatric population the overall incidence of first treated acute rejection, death, and graft loss were 22%, 1.9%, and 7.2%, respectively, with decreases in the incidence of treated acute rejection and graft loss from 1998-2000 to 2013-2014 (Table 3).

Renal function

The incidence of DGF was 63.3% for standard, 72.1% for expanded deceased donor kidney transplants, and 32.7% for the deceased pediatrics transplants. The proportion of patients with excellent renal function (creatinine < 1.5 mg/dl) at 12 months was 65.4% for living, 64.5% for standard deceased, 38% for expanded deceased and 87.9% for pediatric kidney transplant recipients. The proportion of patients with excellent renal function either increased or remained unchanged comparing 1998-2000 to 2013-2014 (Table 3). The proportion of kidney/pancreas

Table 3 Key efficacy parameters and renal function 1-year after transplantation, according to transplant origin

	Living donors		Standard criteria donors		Expanded criteria donors		Pediatric transplants	
	1998 - 2000 (N = 643)	2013 - 2014 (N = 434)	1998 - 2000 (N = 224)	2013 - 2014 (N = 734)	1998 - 2000 (N = 29)	2013 - 2014 (N = 450)	1998 - 2000 (N = 52)	2013 - 2014 (N = 99)
First treated acute rejection, n (%)	168 (29.1%)	117 (30.1%)	82 (42.3%)	163 (24.6%)	13 (54.2%)	85 (20.8%)	21 (42%)	27 (29%)
Death, n (%)	19 (3.0%)	2 (0.5%)	24 (10.7%)	29 (4.0%)	3 (10.3%)	21 (4.7%)	0 (0%)	2 (2.0%)
Graft loss, n (%)	22 (3.4%)	5 (1.2%)	31 (13.8%)	29 (4.0%)	6 (20.7%)	21 (4.7%)	9 (17.3%)	4 (4.0%)
Lost to follow up, n (%)	26 (4.0%)	17 (3.9%)	1 (0.4%)	20 (2.7%)	0 (0%)	10 (2.2%)	0 (0%)	2 (2.0%)
Creatinine mg/dl, 1 year, n(%)	(N = 576)	(N = 390)	(N = 168)	(N = 637)	(N = 20)	(N = 396)	(N = 43)	(N = 91)
< 1.5 mg/dl	281 (48.8)	245 (62.8)	91 (54.2)	375 (58.9)	7 (35.0)	115 (29.0)	28 (65.1)	76 (83.5)
> 1.5 < 3.0 mg/dl	278 (48.3)	141 (36.1)	68 (40.5)	246 (38.6)	12 (60.0)	241 (60.9)	14 (32.6)	14 (15.4)
> 3.0 < 4.5 mg/dl	15 (2.6)	3 (0.8)	7 (4.2)	12 (1.9)	1 (5.0)	34 (8.6)	1 (2.3)	1 (1.1)
> 4.5	2 (0.3)	1 (0.3)	2 (1.1)	4 (0.6)	0 (0.0)	6 (1.5)	0 (0.0)	0(0.0)

transplant recipients with creatinine < 1.5 mg/dl at one year was similar (89% *vs.* 87%) comparing 2002-2005 and 2014.

Survival outcomes

A progressive increase in five-years patient, graft, and death censored graft survivals were observed comparing 1998-2002, 2003-2006, 2007-2010 and 2011–2014 in living, standard, expanded deceased and pediatric recipients (Table 4). Projected 15-years graft survivals for recipients of living (Figure 2A) and standard deceased donors (Figure 2B.) confirms the trends observed during the first 5 years after transplantation.

Discussion

This large retrospective registry data analysis confirms the premises of the health care model implemented and perfected over the last 18 years. Ultimately, this model allowed the increase of the number of transplants and the shift from living related to deceased donor kidney transplants due to a national and local policy to aprimorate the organ procurement and to promote family organ donation.[6] Importantly, we observed a progressive reduction in the incidence of rejection, graft loss or death from 1998 to 2015, despite unfavorable changes in the demographic characteristics of the population, including increase in donor and recipient age, and in the number of expanded criteria deceased donors.[7]

The growth in the number of deceased donors, as well as the marked progress in dialysis assistance, enabled us to apply more stringent criteria for kidney transplants from living donos.[1,3] These restrictions are based on surgical risk (mortality rate after kidney donation at 3 per 10,000), and uncertainty about the risks of developing chronic kidney disease in the long-term, considering the progressive increase in the life expectancy of the general population.[8]

This cohort analysis included 11,436 kidney transplants, yielding currently more than 8869 patients in regular follow up. The growth of transplants number occurred due to increase in the number of transplants with deceased donors of the last 8 years, as consequence of a competent and systematic public national transplant system funded by the government.[2]

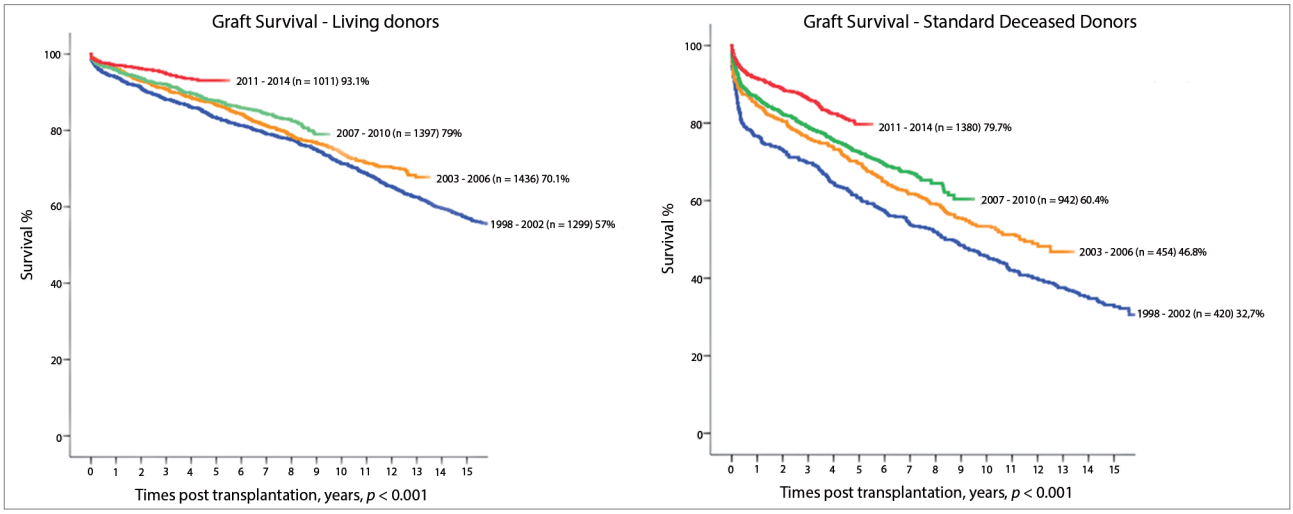
Using more kidneys recovered from expanded criteria deceased donors, that are also increasing worldwide, we also face personal conflicts due to the lack of universal and established criteria to accept or discard these kidneys, despite well-known inferior long term outcomes, and histological analysis before transplant is regularly done.[7]

Overall 38.5% of kidney transplant recipients received tacrolimus, azathioprine and prednisone contrasting with only 0.8% among US centers.[9] Tacrolimus, mycophenolate and prednisone are used primarily in high immunological risk patients, including re-transplants, and in recipients of deceased donor

Table 4 Cumulative 5- years patient, graft and death censored graft survivals for transplants performed between 1998 to 2014

	Patient Survival (%)	Graft Survival (%)	Death censored graft survival (%)
Transplant year			
Living donors			
2011 - 2014 (N = 1011)	97.3	93.1	95.6
2007 - 2010 (N = 1397)	94.0	87.8	93.7
2003 - 2006 (N = 1436)	92.9	86.8	92.6
1998 - 2002 (N = 1299)	92.3	83.3	89.6
StaNdard deceased donors			
2011 - 2014 (N = 1380)	89.2	79.7	90.3
2007 - 2010 (N = 942)	83.7	72.6	87.2
2003 - 2006 (N = 454)	80.5	69.5	87.5
1998 - 2002 (N = 420)	79.7	60.7	77.3
ExpaNded criteria donors			
2011 - 2014 (N = 803)	85.2	71.5	86.0
2007 - 2010 (N = 421)	80.0	59.5	78.6
2003 - 2006 (N = 152)	72.7	58.6	82.0
1998 - 2002 (N = 43)	79.1	46.5	62.8
Pediatric transplants			
2011 - 2014 (N = 220)	97.2	80.9	83.7
2007 - 2010 (N = 240)	96.6	81.2	83.8
2003 - 2006 (N = 213)	93.3	82.8	88.5
1998 - 2002 (N = 135)	99.3	79.8	80.5

Figure 2. A: Cumulative projected 15-years graft survival for recipients of living donor kidney allograft according to 4 transplant periods. B: Cumulative projected 15-years graft survival for recipients of deceased donor kidney allograft according to 4 transplant periods.



expanded criteria kidneys. The progressive use of induction therapy and increased use of tacrolimus and mycophenolate might be associated with the observed reduction in the incidence of treated acute rejection.[10]

Although immunosuppressive regimens with higher efficacy for the prevention of acute rejection might also contribute to improved patient and graft survival, we must consider additional key "increments" that occurred within the last twenty years, including the use of steroid sparing regimens, therapeutic drug monitoring of immunosuppressive drugs, earlier detection of rejection episodes, prophylaxis for a wide range of infections and use of high efficient laboratory techniques for the diagnosis of infections.[11,12]

Renal function at the end of the first year after transplantation has become a biological surrogate marker for long-term allograft survival.[13] Despite the increase in the use of kidneys recovered from expanded deceased donors, we observed a small decrease in the incidence of DGF over time.[14] Importantly, cold ischemia time is still unacceptably high and several measures are been discussed to address this important issue. Reduction in cold ischemia time and in the incidence of DGF, combined with therapeutic immunosuppressive drug monitoring has been associated with superior renal function and graft survival.[15] It is one of the major area for improvements.

The implementation of a dynamic and efficacious local health care program was associated with a progressive increase in the number of kidney transplants, in the cumulative number of patients in follow up and a shift from living related to deceased donor kidney transplants, with progressive increase in patient and graft survivals.

The progressive increase in patient and graft survival has been observed in many other centers and registry analysis.[16] Nevertheless, it is interesting to note that such improvement, comparable with those reported in developed countries, has been observed in a high risk population considering the high incidence and duration of DGF and the poor socio-economic status of the majority of the transplant recipients, a new key variable that has been implicated in the long-term outcomes after transplantation.

All limitations related to registry data analysis also apply to our study, including extrapolation of the data to other populations, even within our country. This analysis was concentrated in major outcomes after kidney transplantation, precluding rigorous statistical analyses and determination of associations or causalities.

In summary, this single center retrospective registry analysis including data from 11,436 consecutive kidney transplants showed that this unique large scale healthcare model provides environmental and administrative conditions to perform and follow a large number of kidney transplants with high efficiency and progressively improvement outcomes. The advantages of this model should be tested in other complex medical therapeutic areas.

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Abbreviations

Anti IL2R: anti-interleukin-2 receptor;
AZA: Azathioprine;
CsA: Cyclosporine;
DGF: Delayed graft function
EVR: Everolimus;
Hrim: Hospital do Rim
MPA: Mycophenolic acid;
OPO: Organ procurement organizations
Pred: Prednisone;
rATG: rabbit antithymocyte globulin;
SRL: Sirolimus;
SUS: Sistema Único de Saúde
TAC: Tacrolimus

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