Kidney transplantation in Brazil and its geographic disparity

O contexto do transplante renal no Brasil e sua disparidade geográfica

Authors

José O. Medina-Pestana[1]
Nelson Zocoler Galante[1]
Hélio Tedesco-Silva Jr.[1]
Kelly Miyuki Harada[1]
Valter Duro Garcia[2]
Mário Abbud-Filho[3]
Henry de Holanda Campos[4]
Emil Sabbaga[5]

[1]Universidade Federal de São Paulo – UNIFESP.
[2]Santa Casa de Misericórdia de Porto Alegre.
[3]Faculdade de Medicina de São José do Rio Preto – FAMERP.
[4]Universidade Federal do Ceará – UFC.
[5]Universidade de São Paulo – USP.

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Correspondence to:
José O. Medina-Pestana
Rua Borges Lagoa, 960, 11° andar – Vila Clementino
São Paulo – SP – Brazil
Zip code 04038-002
E-mail: medina@hrim.com.br

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Abstract

The Brazilian National Transplantation System coordinates and regulates perhaps the largest public transplantation program worldwide. Since its implementation in 1997, the number of kidney transplantations increased from 920 (5.8 pmp) in 1998, to 4,630 (24.1 pmp) in 2010. This growth was primarily due to the increased number of effective donors (from 1.8 pmp in 1998 to 9.3 pmp in 2010), with a corresponding increased number of kidneys transplanted from deceased donors (3.8 pmp in 1999 *versus* 9.9 pmp in 2010).The number of kidney transplantations from living donors has not increased significantly, from 1,065 (6.7 pmp) in 1998 to 1,641 (8.6 pmp) in 2010, either as a consequence of the observed increase in the deceased donor program or perhaps because of strict government regulations allowing only transplantations from related donors. From 2000 to 2009, the mean age of living donors increased from 40 to 45 years, while it increased from 33 to 41 years for deceased donors, of whom roughly 50% die of stroke. There are clear regional disparities in transplantation performance across the national regions. While the state of São Paulo is ranked first in organ donation and recovery (22.5 pmp), some states of the Northern region have much poorer performances. These disparities are directly related to different regional population densities, gross domestic product distribution, and number of trained transplantation physicians. The initial evaluation of the centers with robust outcomes indicates no clear differences in graft survival in comparison with centers in the USA and Europe. Ethnicity and time on dialysis,

Resumo

O Sistema Nacional de Transplantes (SNT) Brasileiro coordena e regulamenta o, provavelmente, maior programa de transplantes públicos do mundo. Desde o seu estabelecimento, em 1997, o número de transplantes renais aumentou de 920 (5,8 pmp), em 1988, para 4.630 (24,1 pmp), em 2010. Esse crescimento foi primariamente devido ao aumento no número de doadores efetivos (de 1,8 pmp em 1998 para 9,3 pmp em 2010), com aumento correspondente no número de rins transplantados de doadores falecidos (3,8 pmp em 1999 *versus* 9,9 pmp em 2010). O número de rins transplantados com órgãos de doadores vivos não aumentou significativamente, 1.065 (6,7 pmp), em 1998, para 1.641 (8,6 pmp), em 2010, tanto em consequência do melhor desempenho do programa de doadores falecidos, como talvez também devido a mais restrita regulamentação, permitindo apenas doação entre doadores vivos relacionados. De 2000 a 2009, a idade média dos doadores vivos aumentou de 40 para 45 anos, e a dos doadores falecidos, de 33 para 41 anos, com eventos cerebrovasculares sendo responsáveis por 50% dos episódios de óbito atualmente. Existem disparidades geográficas evidentes nos desempenhos entre as 5 regiões nacionais. Enquanto o estado de São Paulo ocupa a primeira posição em doação e captação de órgãos (22,5 pmp), alguns estados da região Norte apresentam pequena ou nenhuma atividade de transplante. Essas disparidades estão diretamente relacionadas à densidade populacional regional, ao produto interno bruto e ao número de médicos com treinamento em transplante. A avaliação inicial de desfechos clínicos robustos não indica diferenças nas sobrevidas do enxerto em comparação com as

but not the type of immunosuppressive regimen, decisively influence the measured outcomes. Since the implementation of national clinical research regulations in 1996, Brazilian centers have participated in a number of national and international collaborative trials for the development of immunosuppressive regimens. Besides the challenge of reducing the regional disparities related to access to transplantation, further improvements can be obtained by the creation of a national registry of the outcomes of transplanted patients and living donors, and also by the promotion of clinical and experimental studies to better understand the transplantation-related immune response of the Brazilian population.
Keywords: Organ Transplantation. Legislation, Health. Health Services. Epidemiology. Kidney Transplantation. Immune Tolerance.

observadas nos EUA e na Europa. A etnia e o tempo em diálise, mas não o tipo de imunossupressão, apresentam influência decisiva nos desfechos medidos. A regulamentação nacional da pesquisa clínica foi implementada a partir de 1996, permitindo a participação de centros brasileiros em numerosos estudos clínicos nacionais e internacionais para o desenvolvimento de regimes imunossupressores. Acompanhando o desafio de atenuar as disparidades regionais no acesso ao transplante, o sistema pode ser aperfeiçoado pela criação de um registro nacional para receptores de transplante e de doadores vivos de rins e também pela promoção de estudos clínicos e experimentais voltados a melhor compreender a resposta imune relacionada ao transplante em nossa população.
Palavras-chave: Transplante de Órgãos. Legislação Sanitária. Epidemiologia dos Serviços de Saúde. Transplante de Rim. Tolerância Imunológica.

Introduction

The Brazilian public health system is characterized by free universal coverage, which includes full ambulatory and hospital medical care along with provision of several drugs, including those listed in the exceptional drug program, part of the high-complexity outpatient treatment of rare or low-prevalence diseases (MS/SAS Ordinance nº 105, from 29/03/99).[1] Two internationally acknowledged areas belong to this program: organ transplantation and treatment of carriers of the human immunodeficiency virus (HIV).

The national organ transplantation program is probably the largest public transplantation program worldwide, with a fair organ allocation logistics devoid of social or cultural privileges. The Ministry of Health (MoH) earmarks approximately one billion reais for the program each year, the money being spent on organ procurement, hospitalization for the surgical procedures, hospital readmissions for complications, outpatient follow-up and provision of immunosuppressors. Over 95% of the transplantations are performed within the Brazilian Unified Health System (*Sistema Único de Saúde* – SUS), patients` follow-up being generally the responsibility of the transplantation teams. A recent ordinance has regulated the yearly follow-up of organ donors, determining that coverage be equivalent to an outpatient consultation of a transplant recipient.[2]

Development of the Transplantation National System (Sistema Nacional de Transplantes – SNT)

Since its creation, in 1997, the Brazilian transplantation organization and legislation have been improved and regulated, with the yearly establishment of a decentralized network of collaborators, divided in three fully integrated hierarchical levels: 1 national level (MoH, in Brazilia); 2 regional level, within the structure of each State Health Authority; 3 intra-hospital level (Figure 1). At the national level, the transplantation program is coordinated by the SNT, which is housed in the MoH in Brazilia, having been regulated by the Law nº 9434, from 04 February, 1997. The SNT accredits teams and hospitals for the peformance of transplantations, defines financing and oversees ordinances regulating the process, from organ harvesting to the follow-up of transplant recipients. The SNT coordinates the National Central for Organ Notification, Harvesting and Distribution (*Central Nacional de Notificação, Captação e Distribuição de Órgãos* – CNNCDO), also in Brazilia, and responsible for organ allocation to the states. The SNT also coordinates the State Organ Notification, Harvesting and Distibution Centrals (*Centrais de Notificação, Captação e Distribuição de Órgãos* – CNCDO), belonging to the health authorities of the 27 states.[3] On the regional level, the state centrals coordinate the transplantation activities within the state, registering and ranking the recipients, receiving notifications of potential donors and coordinating the whole logistics process, from diagnosis of brain

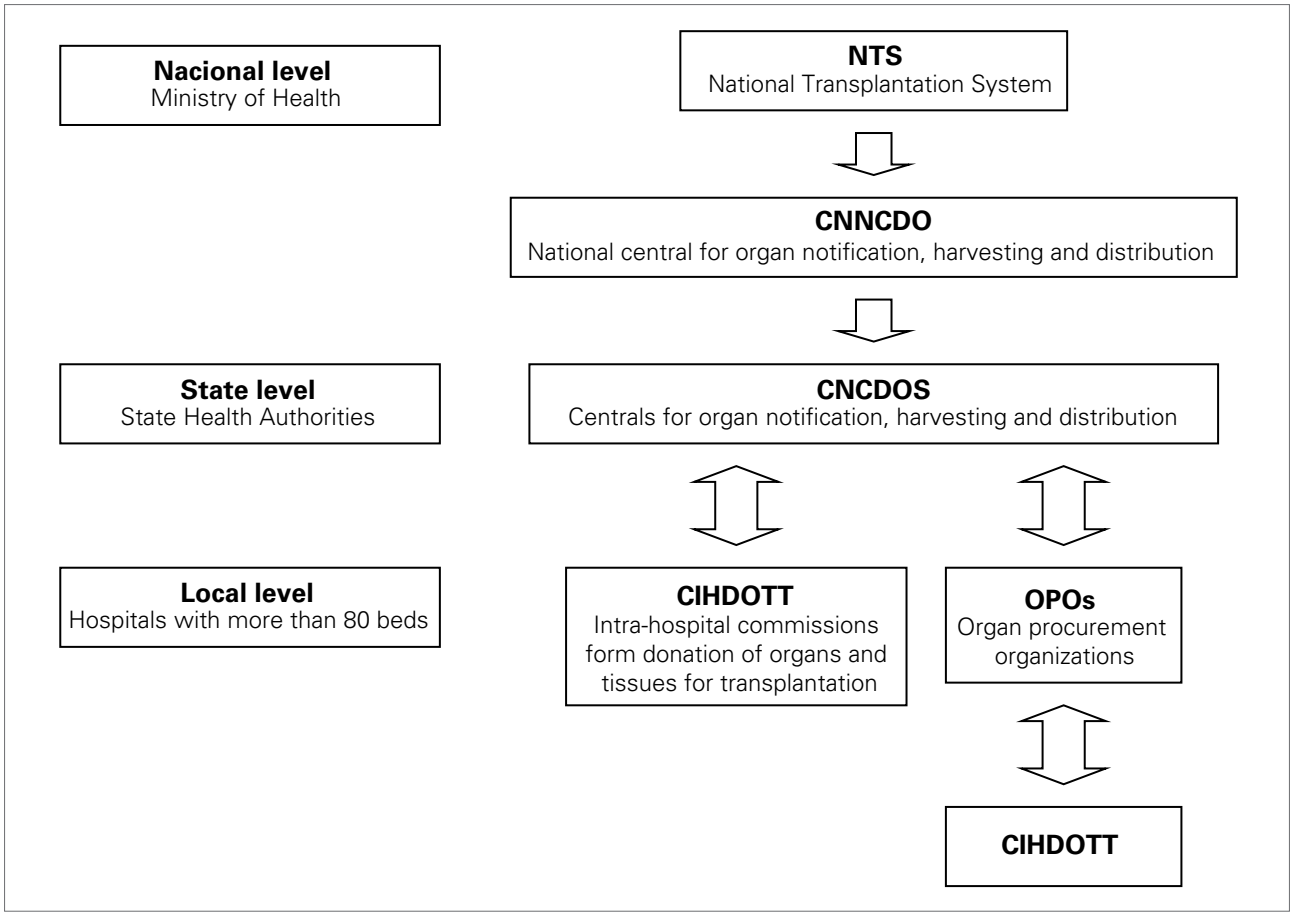
death, through the approach to the donor`s family , to organ harvesting and allocation. The state health authorities may create organ-procurement organizations (*organizações de procura de órgãos* – OPO), also called Organ and Tissue-Procurement Services (*Serviços de Procura de Órgãos e Tecidos* – SPOT), regionalizing organ harvesting in densely populated states or in those with a large geographical area. The densely populated São Paulo state (40 million inhabitants) has 6 SPOTs, 4 in the capital only.

Among the several measures implemented to increase the number of potential donors, the 1997-2001 period saw the regulation of organ harvesting from dead donors based on presumed consent, according to which, only individuals who had expressely registered, in life, their wish not to donate, were not considered potential donors. This way to obtain the family`s authorization for organ harvesting brought discomfort to the population and was later revoked.[4,5]

Between 2001-2010, the family consent for organ donation having been re-established, there was a large increase in the absolute and relative numbers of transplantations from deceased donors, which was the result of a series of other government measures and regulations, and of the positive incorporation of the transplantation program image into the society`s culture. A significant advance in the process of organ harvesting happened following the MoH ordinance nº 1.752, from 23 September, 2005, which determined that every hospital with more than 80 beds should have an organ donation and tissue transplantation internal commission (*Comissão Intra-Hospitalar de Doação de Órgãos e Tecidos para Transplantes* – CIHDOTT), with the aim of proactively detecting potential donors.[6] Brazil has 6,489 hospitals (of which, 154 are university hospitals), about 2,000 having more than 80 beds. Of these, 561 have already defined their internal commissions. Most of these CIHDOTTs are concentrated in Southeastern Brazil, 221 being located in São Paulo state.[7]

An event which occurred in October 2008, in Santo André, within the São Paulo metropolitan region (the Eloá case), was an example of the need to make the population aware of the importance and seriousness of the national program of organ transplantation.

Figure 1. Organization of the national transplantation system.



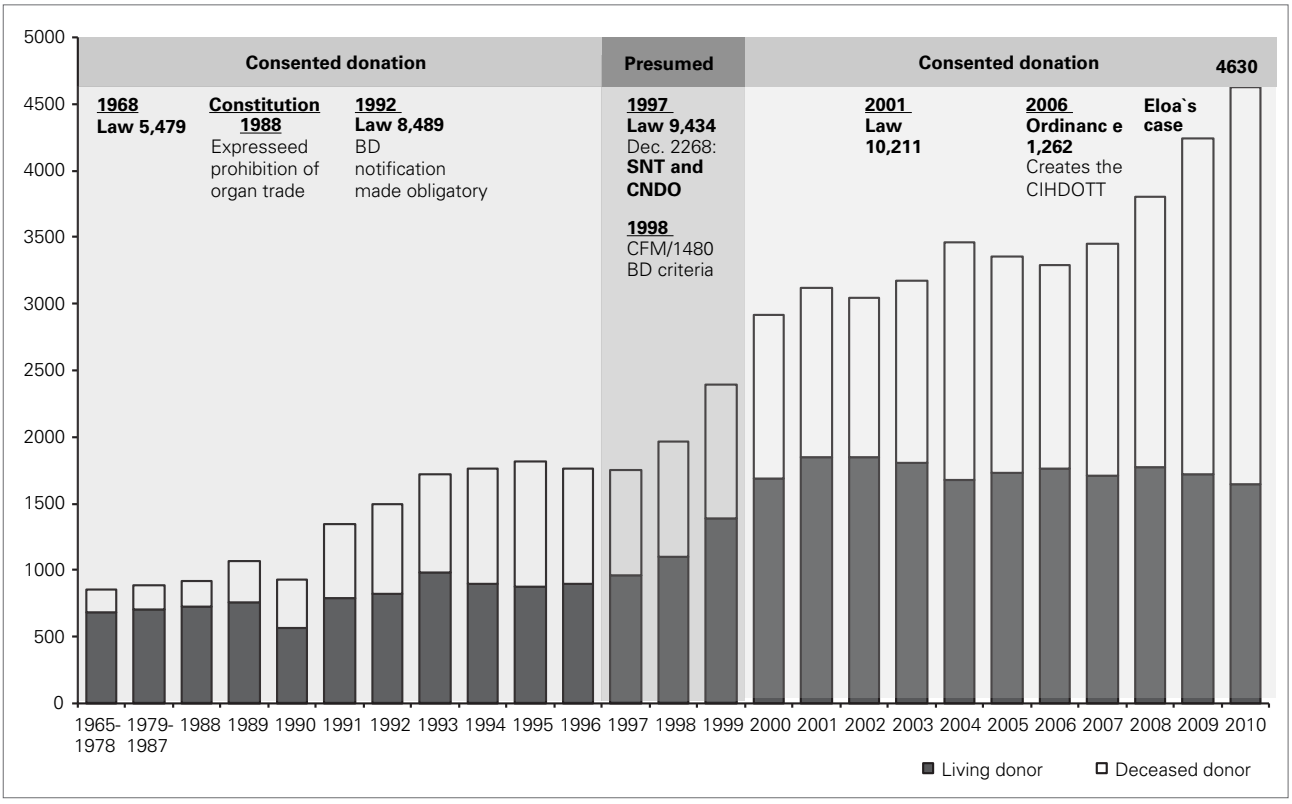
This event contributed to the understanding of the donation process, as it generated more than 90 thousand pieces of news in 15 days, with permanent media coverage of the facts that led to the death of a 15-year-old girl with subsequent organ donation. All medical interventions implemented to avoid the death of the patient, who had suffered a gunshot-induced cranioencephalic trauma, the means used to diagnose brain death, the process of approaching the family and counseling it on the donation issue, the family decision, the logistics of organ harvesting and allocation to a single list, the destination of the organs to different institutions according do the first compatible receptor on the waiting list (regardless of the receptor`s origin) were all widely broadcast. Whether by coincidence or not, the number of donors in São Paulo has significantly increased after that event.

The positive results of the investment and advancement of the transplantation legislation have been clearly demonstrated by the evolution of the national performance in the past few years. The number of transplantations has increased from 920, in 1988, to 1,722 (in 1993), 2,394 (in 1999), 3,466 (in 2004) and 4,630 (in 2010).[8] The living donor/deceased donor ratio remained close to 50% between 1994 and 2007. In the past 3 years, the rate of transplantations from deceased donors has substantially increased, more than 70% of renal transplants in 2010 coming from this source (Figure 2).

The need for transplantations

The estimated need of organ transplantations per million inhabitants and the number of transplantations performed in 2010 are shown in Figure 3. The number of people presently awaiting transplantation are 34,640 (kidney), 4,304 (liver), 576 (pancreas-kidney), 305 (heart) and 161 (lung). In several Brazilian states, like São Paulo, there is no waiting list for corneal transplantation, which must soon be the countrywide situation, as there is no age limit for cornea donation, and the cornea can be removed from almost all donors up to 6 hours after death. The large and increasing number of subjects in the kidney transplantation waiting list is due to the progressive improvement of the quality of life and increased life expectation afforded by dialysis, this therapeutic option being even better for certain patient groups.[9] Heart, liver and lung transplantations are indicated for patients whose life expectation, as related to the failing organ, is below 30 months,

Figure 2. Number of kidney transplantations and Brazilian legislative chronogram during the 1965-2010 period



BD: brain death; SNT: national transplantation system; CNCDO: centers of organ notification, harvesting and distribution; CFM: Federal Medical Council; CIHDOTT: intra-hospital commission for organ and tissue donation.

which keeps the list small, in comparison with that of kidney transplantation, in which subjects may be maintained on dialysis for decades.

The demographic profile of candidates to kidney transplantation from a deceased donor, in the São Paulo state, may be representative of the national average. Analysis of 7,123 patients on the kidney transplantation waiting list has shown that 76% of the candidates are between 21 and 60 years of age, and only 51 are under 18, corresponding to fewer than 1.5 candidates at the pediatric age range on the waiting list, per million population.[10]

Organ allocation

The allocation of organs from living or deceased donors is regulated by the SNT. There are no confirmed irregularities concerning organ allocation, from living or deceased donors, any accusation being readily investigated by the Prosecution Office.

The allocation of organs from deceased donors is controlled by the state centrals, the kidneys being allocated according to the best human leukocyte antigen (HLA) matching. Heart, pancreas and lung are allocated according to the time on the waiting list. The liver is allocated to the most severely affected patient on the waiting list, according to the Model for End-stage Liver Disease (MELD) score.[11] For all the organs there are strict circumstantial criteria for priority attribution under extreme situations. Patients with fulminating hepatitis, in cardiogenic shock, without a vascular or peritoneal access for dialysis, or cornea perforation are prioritized to receive liver, heart, kidney and cornea transplants, respectively. Children under the age of 18 years are priorities and compete with adults in all situations, having absolute priority when the donor matches their age range.[12]

Figure 3. Annual transplantation need estimated in absolute numbers and per million population (pmp), and number of procedures performed in 2010.

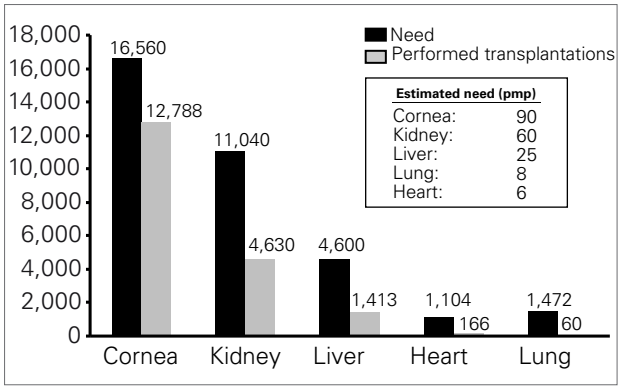
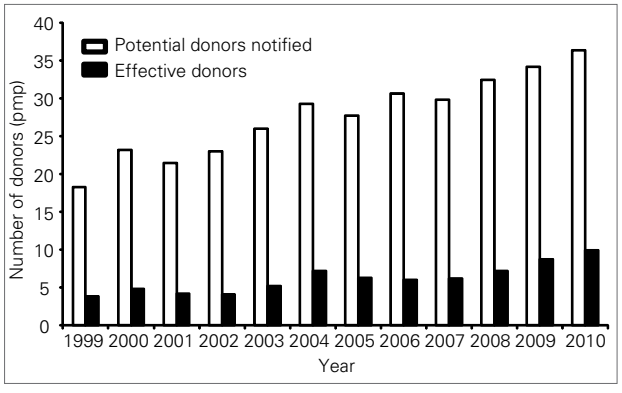
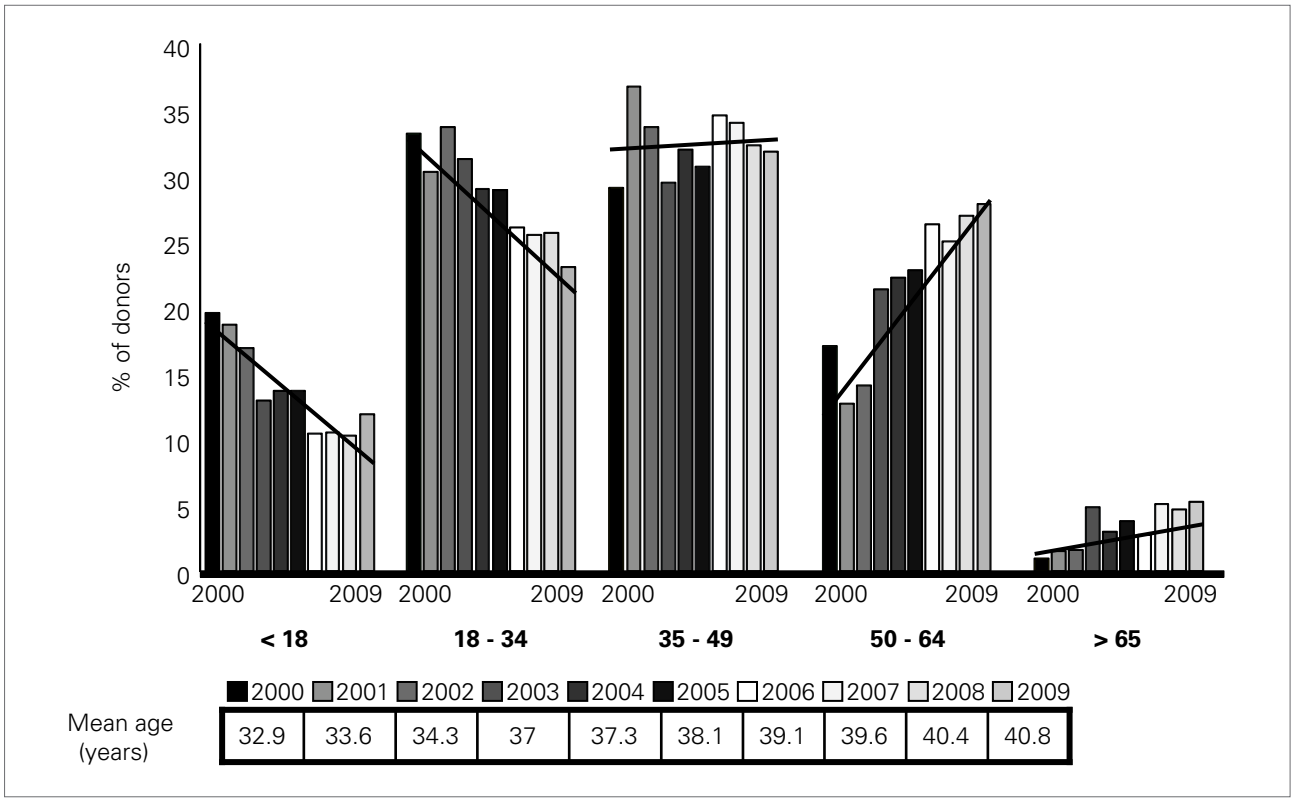


Figure 4. Evolution of organ harvesting in Brazil during the 1999-2010 period.



Between 1999 and 2010, the number of potential deceased donors increased 99%, from 18.3/million population to 36.4/million population. The number of deceased donors increased 160%, from 3.8/million population to 9.9/million population[13] (Figure 4). It must be highlighted that the profile of the deceased donors has progressively changed to become very similar to that from international centers. Data obtained from the São Paulo Health Authority, for the 2000-2009 period, show an increase in the donors` average age, from 33 years, in 2000, to 41 years, in 2009 (Figure 5). There was a progressive reduction in the number of donors aged under 34 years, whose main cause of death is violence,[14] and a proportional increase in the number of donors aged over 50 years, whose main cause of death is stroke. As an example of this shift, the rate of kidney transplantations from expanded criteria donors, defined according to the Organ Procurement and Transplantation Network (OPTN),[15] increased from 4%, in 2000, to 31%, in 2010 at the Kidney and Hypertension Hospital (*Hospital do Rim e Hipertensão*). Of the 158 potential donor notifications received in the first semester of 2010 by the SPOT UNIFESP, 49% of the brain death diagnoses were due to stroke, 27% to cranioencephalic trauma, 18% to anoxia and 5% to other causes. Donation was performed in 40% of the cases, 22% not happening due to lack of authorization by the family. 38% of the potential donors were discarded because of delayed notification, resulting in cardiac arrest before completion of the donation process.[10] Nevertheless, in 2010, only 211 kidneys (12.8%) were rejected as inadequate for transplantation, due to impaired kidney function or histology. This rejection rate is lower than that in the United States and Spain, where rejection rate is over 20%.[16,17] Faster notification of potential donors must not only increase the rate of peformed donations, but

Figure 5. Distribution of donors according to age range in the 2000-2009 period in São Paulo state.

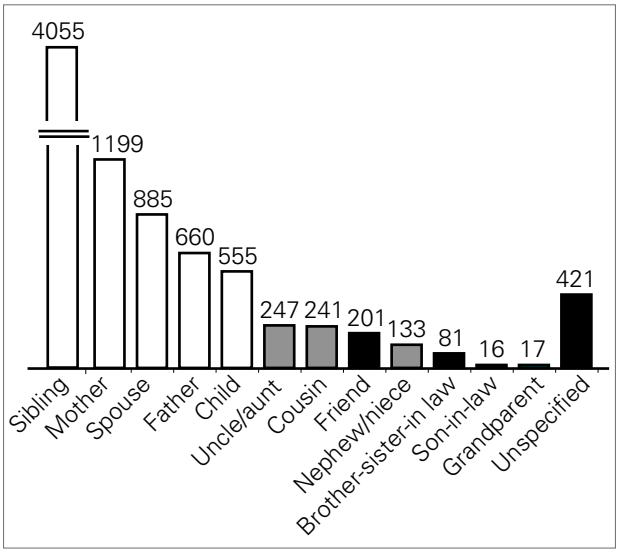


also improve donor maintenance, increasing the viability and fuinctional quality of the harvested organs, and possibly reducing even more the rejection rate.

The allocation of organs from living donors allows transplantations from up to fourth-degree relatives (first-degree: parents and children; second degree: grandparents and siblings; third-degree: uncles, aunts, nephews and nieces; fourth degree: cousins and children from consanguineous uncles and aunts), and also from spouses. Transplantation from unrelated living donors or friends is only allowed after extensive legal analysis, involving medial justification and ethical and judicial authorization. The result of this legislation can be seen in Figure 6, which shows donors` kinship in 8,711 transplantations performed between 2005 and 2009 in Brazil. Whereas most these transplantations were performed between siblings, parents and spouses, only 201 (2.3%) kidney transplantations were performed with kidneys from friends.

Sensible definition and approach to the selection of a live donor are essential for the donor`s safety. Besides the standard clinical and laboratory assessments, the birthweight should be considered, as low birthweight is related to renal function decline later in life,[18] and the presence of microalbuminuria, more common in those with a single kidney, is an isolated risk factor for the development of cardiovascular disease.[19]

Figure 6. Kinship between donors and recipients of 8,711 kidney transplantations performed in the 2005-2009 period in Brazil.



In spite of the growing gap between the number of donors and the number of potential recipients on the waiting list, organ donation from children to parents, around 100 donors/year (Figure 6), should be questioned and intensely debated. Young age at the time of donation, the increasing life expectation and the hereditary nature of many renal diseases are risk

factors that may be associated with the development and faster progression of renal dieases in donors with a single kidney. This same concept must be employed in the selection of young donors who have a parental history of hypertension, diabetes mellitus or early cardiovascular disease, and who may develop more accelerated renal disease after donation.

The same profile shift toward an older donor age has been observed among living donors, with increasing use of organs from older living donors. The mean age of living donors increased 5 years in the last decade, from 40 to 45 years, living donors over the age of 70 years being frequently found.[10] The oldest donor at the Kidney and Hypertension Hospital, who donated a kidney to her son, at the age of 81, is now 91 and remains healthy.

Because there is no Brazilian registry of kidney donors, it is impossible to assess the repercussions of nephrectomy on the function of the remaining kidney and on the donor´s survival in the long run. The living donor must be regularly followed up and counseled on hazards such as overweight, hypertension, smoking and other habits associated with a higher risk of development and progression of renal and cardiovascular disease.

Regional disparities in the number of transplantations

Although the well established logistics of the SNT has resulted in increasing transplantation numbers, there are striking regional disparities. Whereas the performance of São Paulo, the Federal District, Rio Grande do Sul and Santa Catarina, as regards organ harvesting, is close to that of countries with solid programs, in other states, such as Amazon, no organ harvesting from deceased donors occurs.

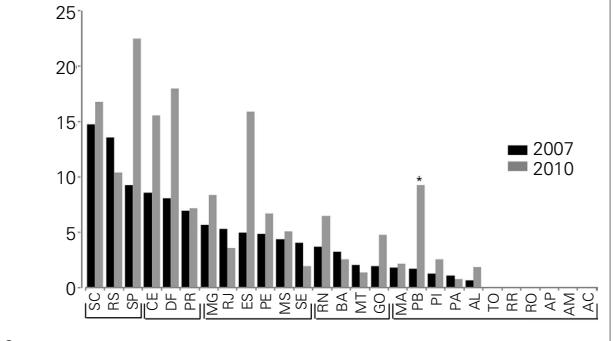
In 2007, the average number of deceased donors was 6.2/million inhabitants, ranging from 0 to 14.8 countrywide. Based on these results, the states were grouped according to five categories of organ harvesting performance: I, states with 9-25 effective donors/million inhabitants; II, with 6-9 donors; III, with 4-6; IV, with 2-4; and V, with 0-2 (Figure 7). Starting from these figures, goals for the number of deceased donors were set for the next three years. The three states with more than 10 donors/million inhabitants maintained or increased the number of effective donors (Santa Catarina, São Paulo and Rio Grande do Sul), with three states showing a decline (Rio de Janeiro, Mato Grosso and Sergipe). The performance of Paraíba state, with 3.7 million inhabitants, and which jumped from category V to category I in three years is noteworthy. This exceptional evolution was due to the action of the state government and commitment of the harvesting teams, which liaised to reach the proposed goal.

Analysis of kidney transplantations performed in 2009 in each geographic area showed that most occurred in Southern and Southeastern Brazil. These regions concentrate 57% of the Brazilian population, 73% of the Gross Domestic Product (GDP) and most professionals affiliated to the Brazilian Transplantation Society (*Associação Brasileira de Transplantes de Órgãos* - ABTO)[8] (Figure 8). These demographic and socioeconomic characteristics directly influence the number of indexed scientific publications on organ transplantation, 80% of which, in the past 10 years, came from the Southeast, only 16% coming from the South and 4% from the other regions.

The São Paulo model

The commitment of the São Paulo government to the transplanation program and the reduction of obstacles to efficiency were fundamental for the results already observed in the state. The state concentrates 22% of the Brazilian population, and 34% of the GDP. Of the 561 CIHDOTTs already set in the country, 221 are in São Paulo. Furthermore, several initiatives toward

Figure 7. Stratification of the performance of organ harvesting in the Brazilian states, according to the rate of effective donors per million inhabitants in 2007. The growth goals for 2010 were set from the performance of each state in 2007.

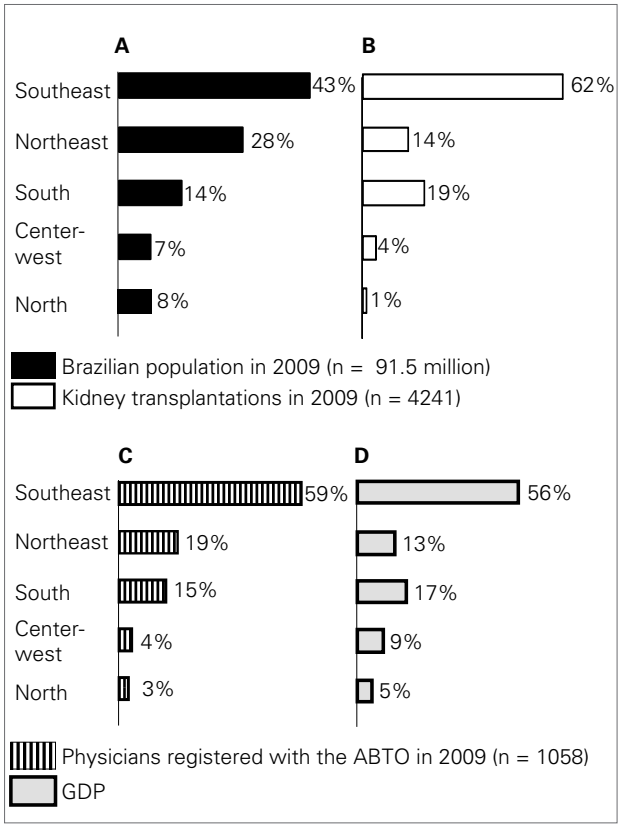


Category	I	II	III	IV	V
Performance 2007	9 - 25	6 - 9	4 - 6	2 - 4	0 - 2
2010 Goal	≥ 25	≥ 10	≥ 7,5	≥ 5	≥ 3

*Paraíba state increased from 1.7 to 9.3 donors per million inhabitants in 3 years.

identification of potential donors and performance of organ donation have been implemented since 2007 (Table 1). The results have been observed in the past three years, period during which the number of effective donors increased from 10 to 21.2/million inhabitants, resulting in 1,439 kidney transplantations performed in 2010. This performance is superior to the national average and close to the averages of the countries with the best performances at present: the United States, Portugal and Spain[20] (Figure 9). The number of kidney transplantations from living donors is equivalent to that of the United States, and the total number of kidney transplantations, from deceased and living donors, is 52/million inhabitants, close to the estimated 60/million inhabitants/year. The result of the interventions implemented in this state demonstrate the growth potential of the national transplantation program, and the possibility of reaching the necessary number of transplantations/million inhabitants/year in the whole country.

Figure 8. Percentage distribution of the Brazilian population (A), kidney transplantations (B), physicians registered with the Brazilian Society of Organ Transplantation (C) and Gross Domestic Product (D), according to the 5 Brazilian gepographical regions.



ABTO: Brazilian Association of Organ Transplantation; GDP: Gross Domestic Product.

Survival of kidney transplant recipients

After consolidation of the national transplantation program, with implementation of measures to increase its efficiency and the number of deceased donors and establishment of a yearly registry of all activities related to organ and tissue transplantation, the ABTO now embarks on a new stage of critically assessing transplantation performance in the country. Nationwide data and data from the kidney transplantation centers show increased patient and graft survival, a result of consolidation of the system (Figure 10).[21-24] Allocation of HLA-matched kidneys from deceased donors has increased graft survival in the long run. In São Paulo state, the survival of grafts from deceased donors without HLA-A, HLA-B and HLA-DR mismatches was 77.3% by the end of 5 years of follow-up, while that of grafts with the six haplotype mismatches was 70.9%.[10]

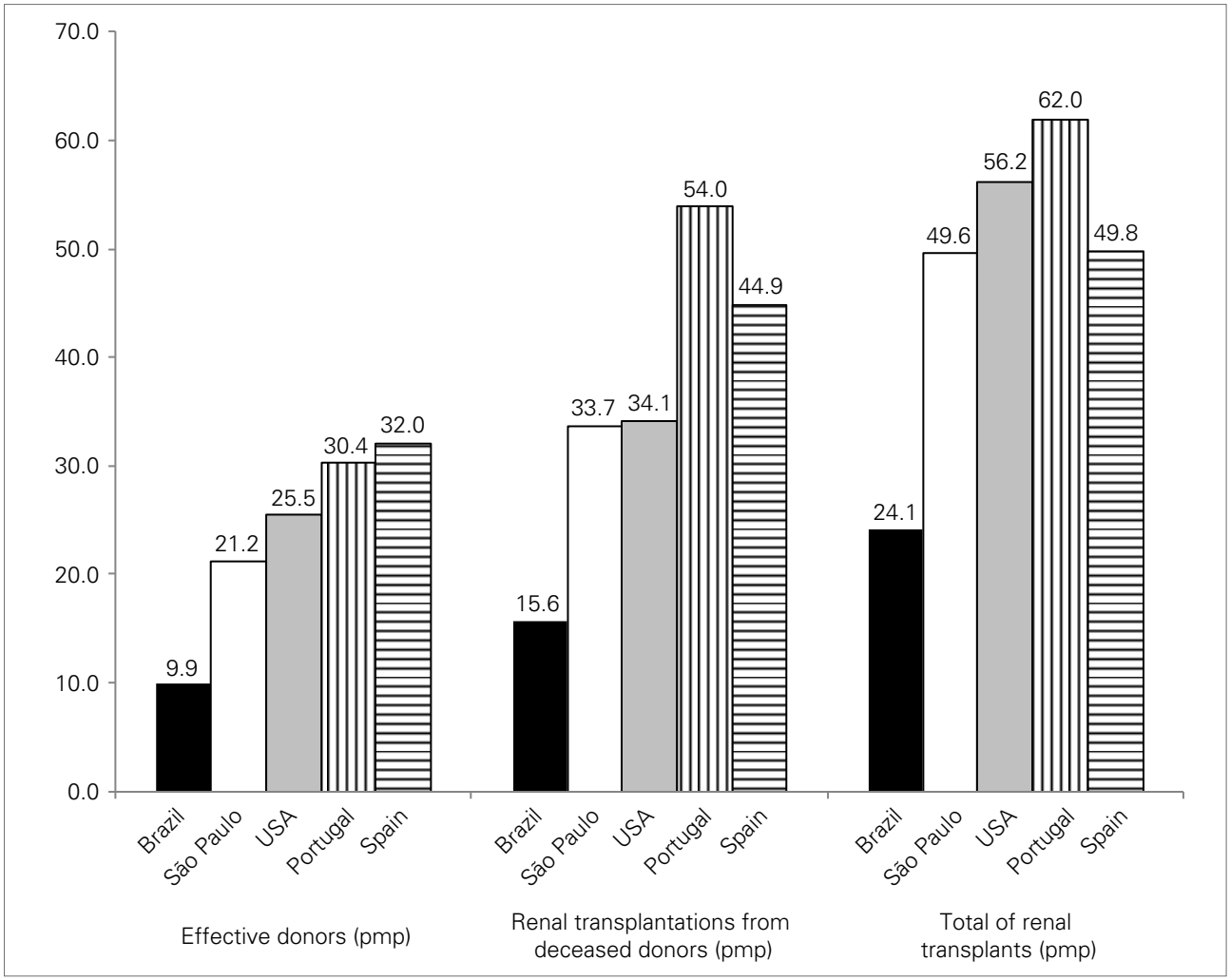
A special effort should be made to develop and apply guidelines to the follow-up of specific groups, such as black recipients, who have a less favorable evolution after kidney transplantation (Figure 11). There is also a need to identify immunosuppressive regimens more suitable to the Brazilian population. Because of the socioeconomic and nutritional features of the population on the kidney transplantation waiting list, and the presence of a number of nationally endemic infections, the decision about the immunosuppressive regimen must

Table 1 List of improvements to organ harvesting promoted by the São Paulo Health Authority since 2007

1. Disponibilization and payment of 7 medical teams for performance of Doppler exams and EEG;
2. Ground transport of the material and team for harvesting outside the municipality;
3. Definition of a support laboratory for serologies;
4. Capacitation and payment of intra-hospital coordinators;
5. Disponibilization of pathology services for assessment of expanded criteria donors;
6. Organization of the CNCDOs with logistic support, trained teams, and internet publication of information;
7. Operational technical support targeting optimization of the performance of the services for organ and tissue procurement;
8. Outcome and survival registry, with the provisioon of data concerning the enrolment of new members in the waiting list.

EEG: Eletcroencephalogram; CNCDOs: Centers for Organ Notification, Harvesting and Distribution.

Figure 9. Comparison of organ harvesting and number of kidney transplantations performed (pmp) in Brazil, São Paulo state, United States, Portugal and Spain.

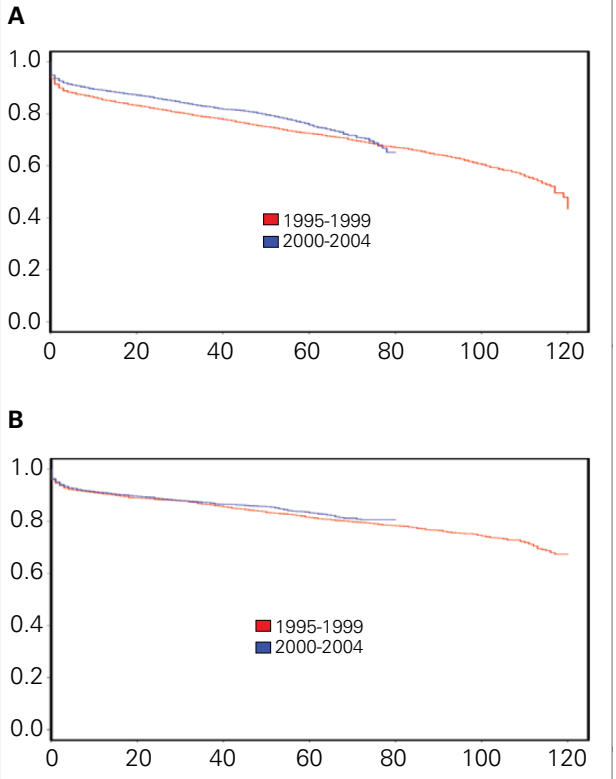


consider not only its efficacy against acute rejection, but also its long-term safety profile. This becomes even more important when recent studies have suggested that there are no patient and graft survival differences between kidney transplant recipients on steroids and azathioprine/tacrolimus or mycophenolate/tacrolimus regimens, pointing to azathioprine as a therapeutic option for selected patients (Figure 12).[25]

Transplantation research in Brazil

Research on transplantation has paralleled the improvement of the transplantation system. The approval of guidelines and norms regulating the development of research involving human beings, by the Brazilian National Heatlth Council (*Conselho Nacional de Saúde* - CNS), in 1996, originated the process of clinical research regulation in the country. Creation of the National Commission of Research Ethics (*Comissão Nacional de Ética em Pesquisa* - CONEP), to establish guidelines, norms and ethical standards, and of institutional Research Ethics Committees (*Comitês de Ética em Pesquisa* - CEP), with the responsibility of directly monitoring the development of projects of research in humans, has widened the opportunities for liaison among the centers and for international collaboration. In 1987, the first phase IV multicenter study was finished in Brazil, and in 1999, the first phase III multicenter study involving two Brazilian centers was concluded. Around 3,000 kidney transplant recipients are now included in national and/or international multicenter studies, definitely situating the Brazilian centers on the international clinical studies stage. Brazilian centers participate in clinical studies involving everolimus,[26-28] FTY720,[29-33] sirolimus,[34-36] mycophenolate mofetil,[37-41] mycophenolate sodium,[42-44] tacrolimus,[45,46] modified-

Figure 10. Graft (A) and patient (B) survival among kidney transplant recipients in Brazil, according to the date of transplantation.



Source: Brazilian Transplantation Registry – 2007 Quantitative analysis.

release tacrolimus,[47,48] valgancyclovir,[49] belatacept,[50] sotrastaurine (clinicaltrials.gov NCT00504543 e NCT01064791) and JAK3 CP690,550 inhibitor (clinicaltrials.gov NCT00483756).

Brazil has also made advances in the development of experimental research projects involving transplantation immunology. The main lines of investigation include methods for the early diagnosis of acute graft rejection,[51-53] non-invasive monitoring of the immune response,[54] advances in the understanding of the molecular and cellular mechanisms involved in the ischemia and reperfusion injury,[55-57] and in human operational tolerance.[58]

Perspectives

Brazil has experimented advances in its social organization, which can be evidenced by an increased life expectation at birth (76 years for women and 69 years for men),[59] a decreased birth rate (reduced from 5.6 to 2.1 in the past 30 years),[60] reduced infant mortality rate, and reduced urban violence and number

Figure 11. Graft survival among kidney transplant recipients from living and deceased donors, at the Kidney and Hypertension Hospital, during the 1999-2008 period, according to recipient ethnicity.

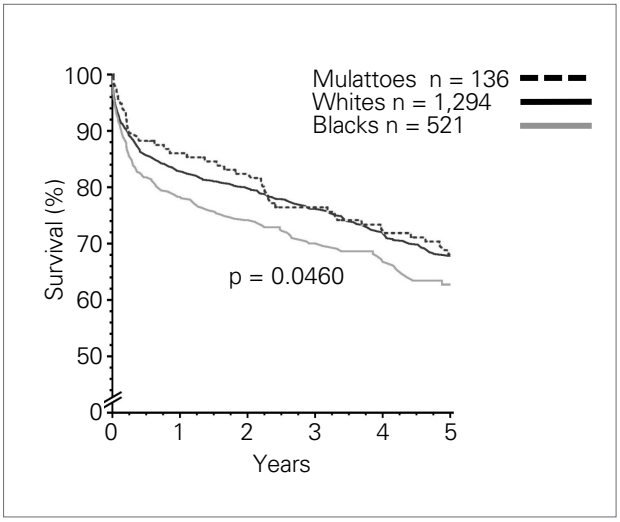
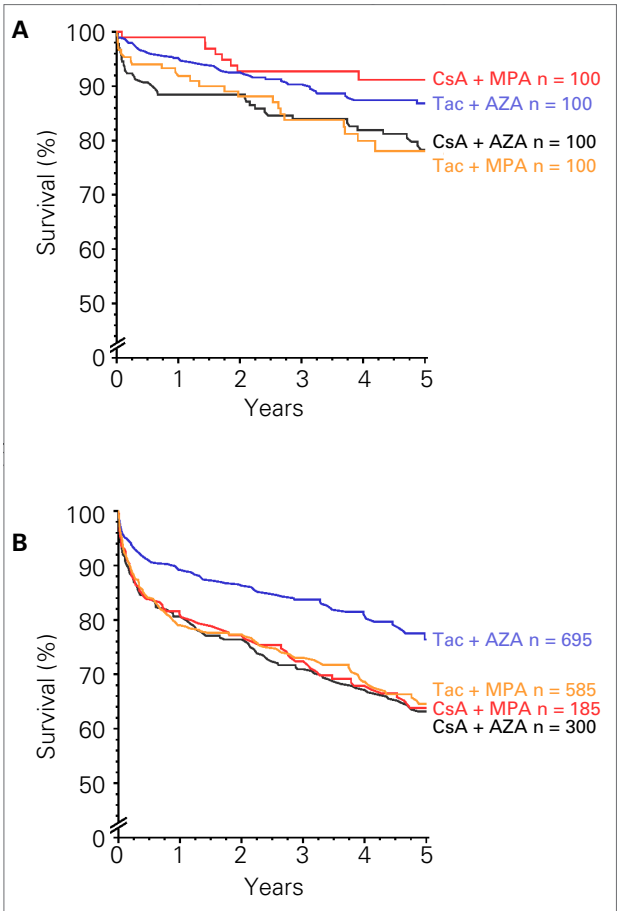
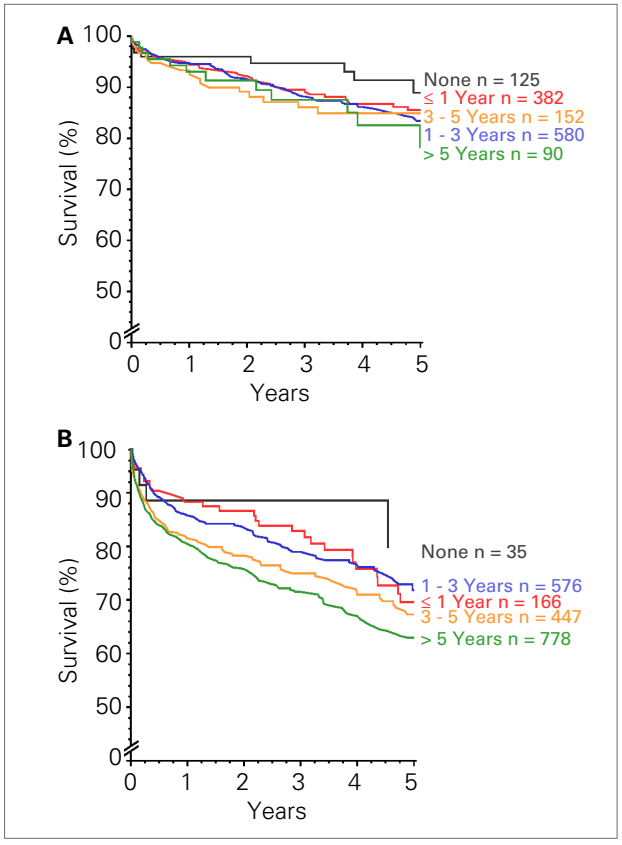


Figure 12. Graft survival among kidney transplant recipients from living (A) and deceased (B) donors, at the Kidney and Hypertension Hospital, according to the immunosuppressive regimen used.



CsA: cyclosporine; Tac: tacrolimus; MPA: mycophenolate; AZA: azathioprine.

Figure 13. Graft survival among kidney transplant recipients from living (A) and deceased (B) donors at the Kidney and Hypertension Hospital, according to time on dialysis.



of violent deaths (from 13,257 in 1999 to 4,436, in 2007, in São Paulo).[61] In this context, the Brazilian transplantation program is an advanced, organized, fair and egalitarian system, that must be preserved as a national high-complexity medical asset and international reference for the Brazilian public health.

This analysis shows a large geographical disparity among the transplantation metric variables, which may be understood as a consequence of the intrinsic regional differences related to access to and quality of health care. This scenery, however, may be changed with commitment from state governments, society in general and transplantation teams. Proof of the effectiveness of these strategies comes from Paraíba state, which experienced a striking increase in the number of transplantations in a short period (3 years), thanks to liaison of the government with the transplantation teams.

In spite of the geographical disparities, the national transplantation program has matured and improved. Besides the continuous effort toward a larger number of donors, several other points must be considered in the process of organ allocation, targeting the improvement of long-term outcomes. Finally, we highlight three needs. Firstly, to support pre-emptive transplantation, once better results have been clearly demonstrated for the population receiving this strategy. While implementation of this strategy may be easier for recipients of living donors, more discussion is necessary for its implementation in patients waiting for an organ from a deceased donor. At present, inclusion in the waiting list is restricted to patients with creatinine clearance under 10 mL/min. Secondly, to better identify and select patients who will experiment real benefits with kidney transplantation in comparison with dialysis (Figure 13). Thirdly, to promote clinical and experimental studies in the Brazilian population to widen our understanding of the immune response and to assess the influence of endemic infections. These approaches may improve the outcomes of specific groups, such as blacks, whose immune response modulation requires greater monitoring.

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